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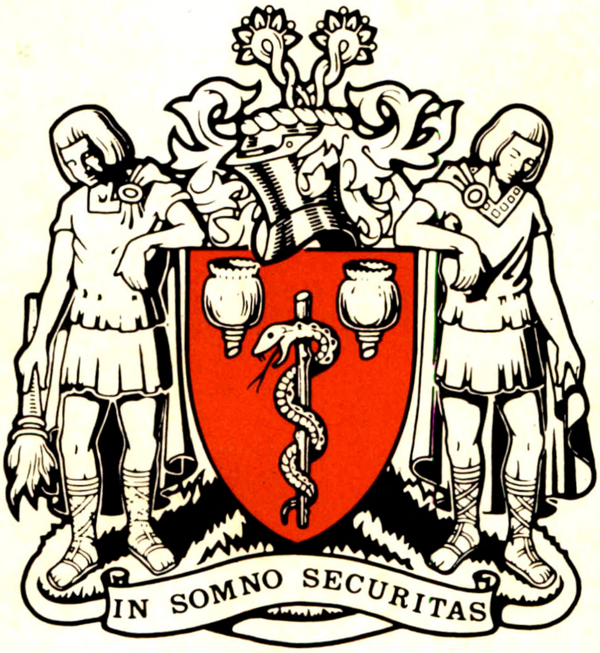

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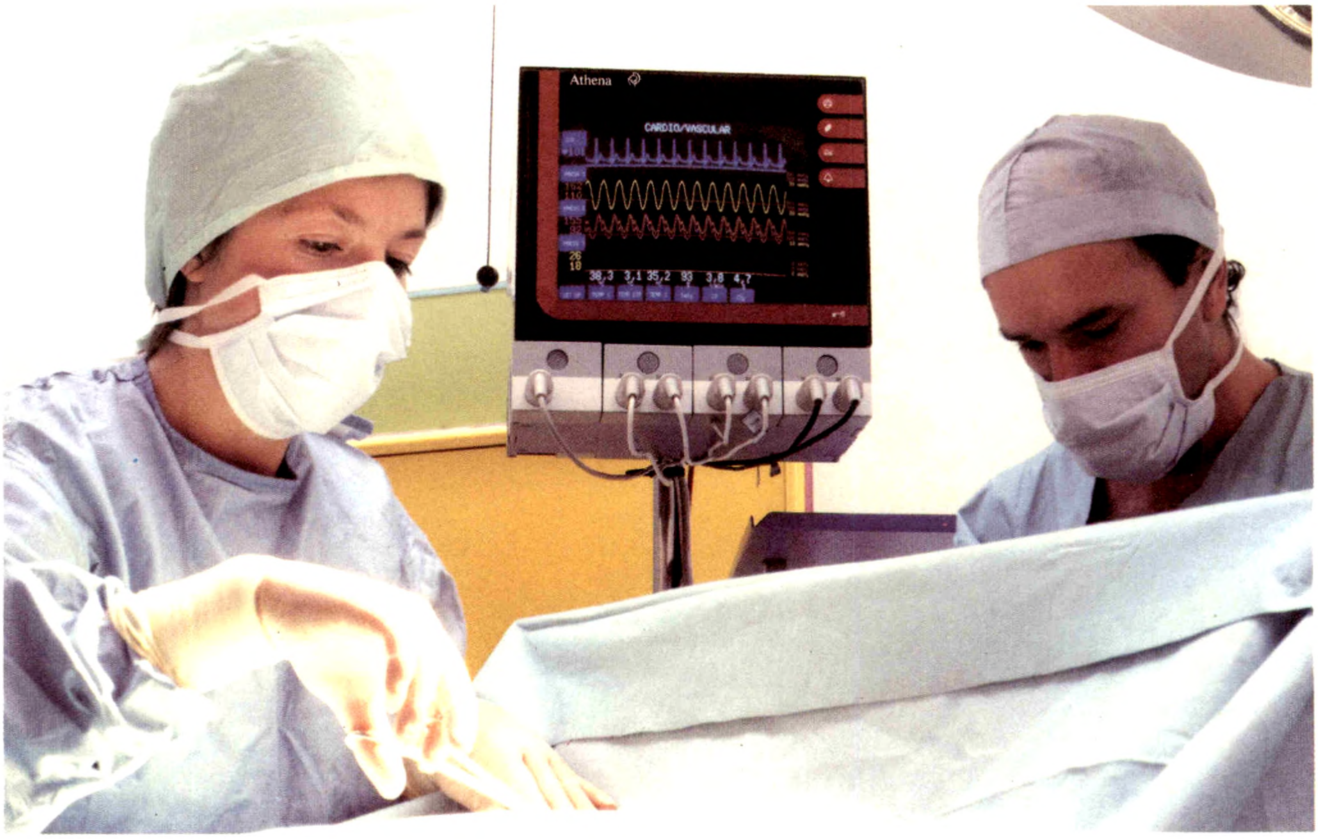

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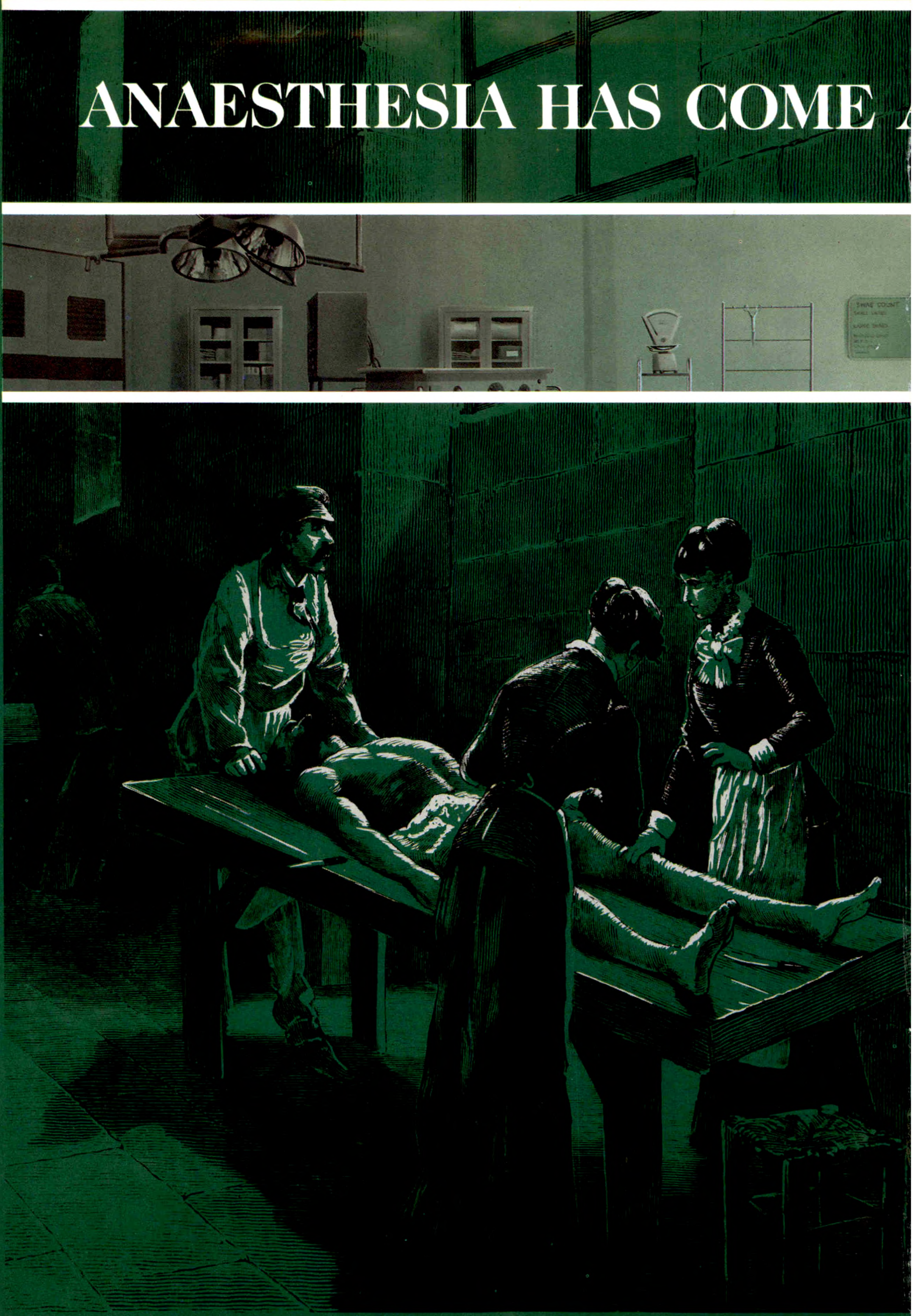

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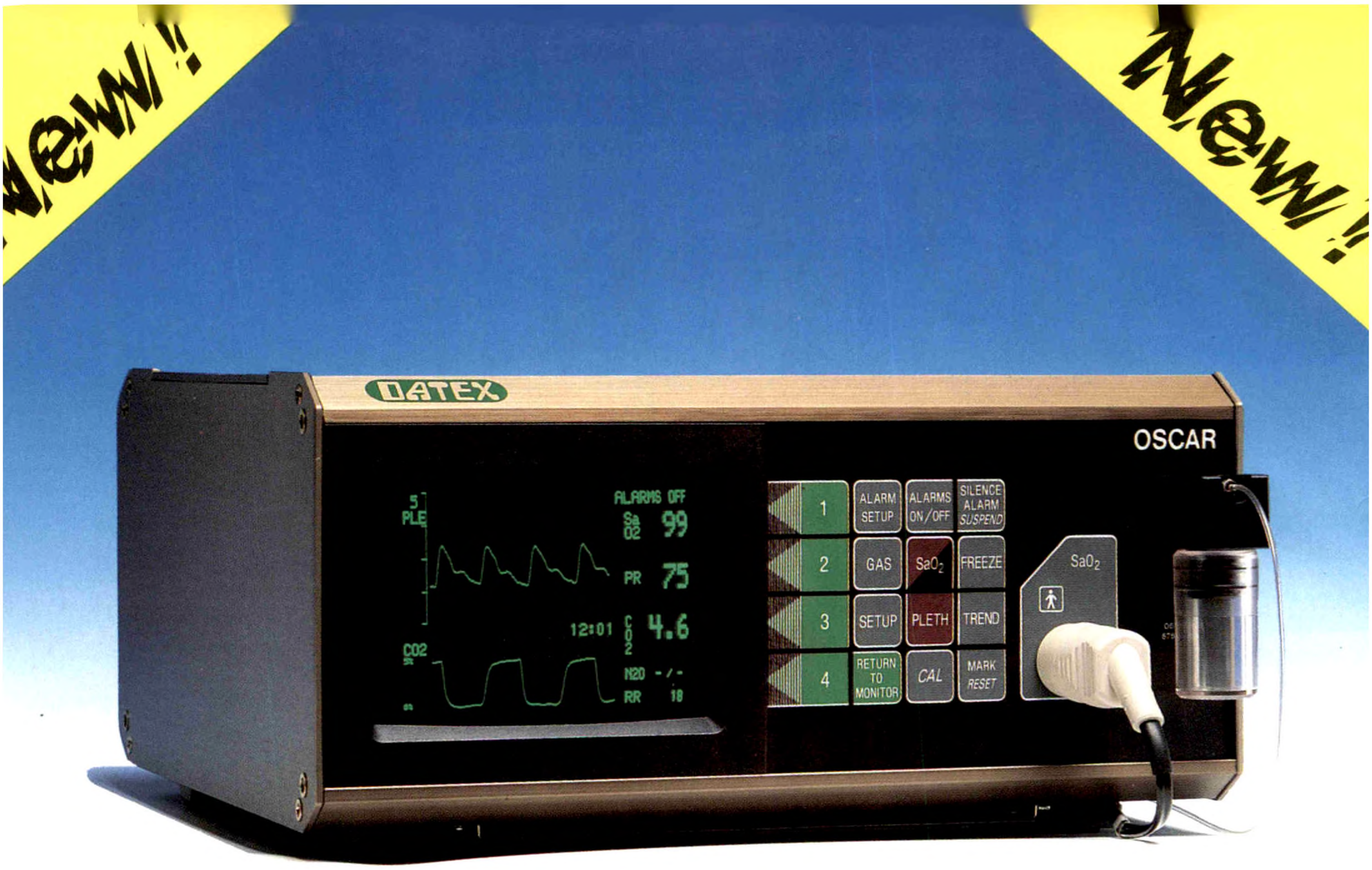

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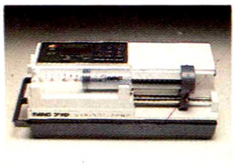

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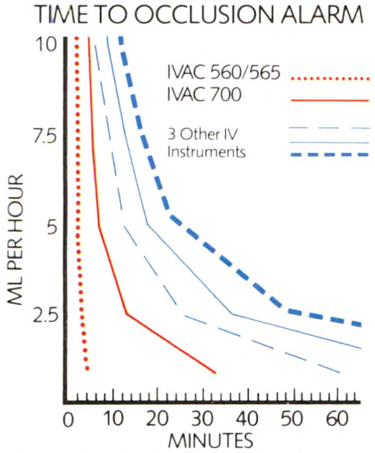

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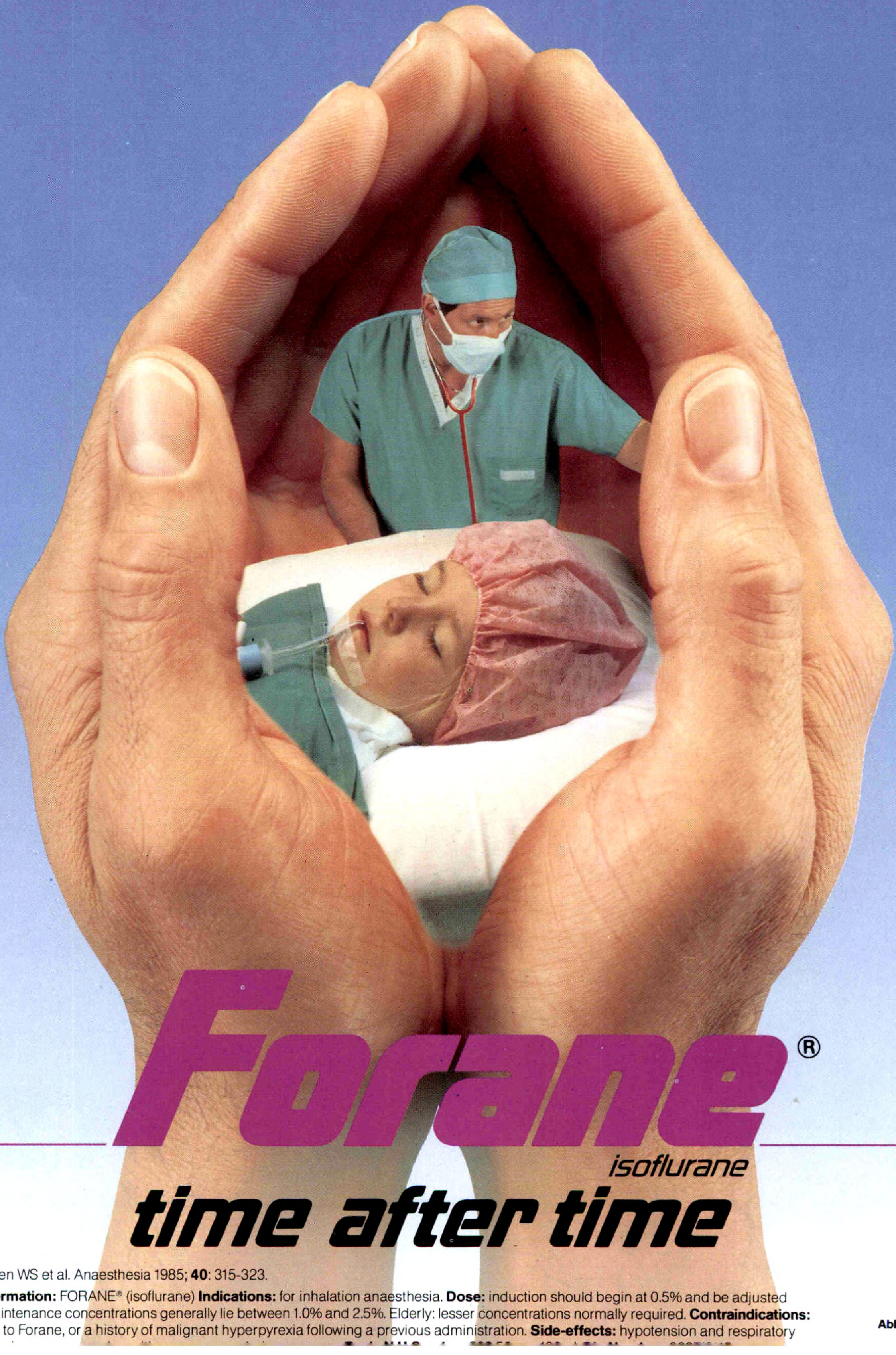
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Anaesthesia, 1988, Volume 43, pages 921–922

Editorial

Vegetative survival after brain insults

Can anaesthetists reduce the frequency of a fate worse than death?

Modern techniques of resuscitation and intensive care now enable many patients to survive acute cerebral insults that would previously have proved fatal. Some make a good recovery but a price is paid by those who are left in what Plum and myself described in 1972 as a persistent vegetative state.[1] This is a high price because once vegetative patients survive for a few weeks they can live for many years, provided they are nursed and nourished. These patients have lost the function of the cerebral cortex but not of the brain stem. They therefore retain a wide range of reflex activity including breathing, swallowing and withdrawal of the limbs from a painful stimulus. There is a diurnal sleep/wake rhythm with the eyes open for long periods, and the eyes may reflexly follow a moving object. But there is no evidence of any psychologically meaningful response and no evidence of a working mind. It is now widely accepted that survival in this state is worse than death. Patients who survive long enough for negligence or malpractice to be proved in relation to the causative event are commonly awarded much higher sums in damages than if they had died. In his address to the Anaesthetic Section of the Royal Society of Medicine in 1981 Lord Scarman said: 'It is much cheaper to kill than to disable and it may be more merciful.'

Insults that can lead to the vegetative state include severe head injury, bilateral brain stem stroke, hypoglycaemia and systemic hypoxic–ischaemic events. The latter can result from myocardial infarction, respiratory obstruction or failure, or hypotension due to haemorrhage or induced by drugs; they may or may not be associated with cardiac arrest. Most hypoxic insults have occurred in hospital, frequently in the course of diagnostic or therapeutic procedures and often under anaesthesia. How many vegetative patients result from spontaneously occurring events, as distinct from those associated with medical interventions, is almost impossible to discover. This is because they occur across a wide range of specialties, although almost all have been in an intensive care unit in the early stages. In the Glasgow-based study of severe head injuries in three countries 5% of 1000 survivors at 6 months were vegetative. In the Anglo-American study of 500 patients with nontraumatic coma 195 survived the acute stage of whom 31% were vegetative.[2] There were 210 with hypoxic ischaemic cerebral insults (150 cardiac arrests, 38 hypotension, 22 respiratory arrests), of whom 58% died; of the survivors 48% were left vegetative and another 23% were severely brain damaged but had regained consciousness.

It ought to be easier to determine the incidence of vegetative survivors after incidents associated with medical intervention. However, formal studies of mishaps usually focus on deaths. In successive studies of peri-operative deaths in the UK, the interval to death has increased from one through 6 to 30 days but this still fails to capture most brain damaged survivors. What is needed is an audit that includes serious complications in survivors, and ideally also 'near-misses', when the patient was not damaged and the doctors breathed a sigh of relief. Investigation of such incidents would not be compromised by the fear of litigation and more might therefore be learnt than from episodes that had resulted in death or disability. Such a study in the Massachusetts General Hospital analysed 359 critical incidents collected on the basis of interviews with anaesthetists; 82% were judged to have resulted from human error. This study concluded that factors that lead to near misses are probably the same as those that result in mishaps that end less happily.[3] Patients who survive following hypoxic incidents, whether with severe brain damage or without any sequelae, are mostly younger and more healthy than those who die within 30 days. This is part of the tragedy, because the comforting finding of the recent enquiry into peri-operative deaths, that either advanced primary disease or serious co-morbidity accounted for most deaths reported,[4] would not apply to most brain damaged survivors. In a prospective survey of almost 200 000 anaesthetics in France only 15 of 67 *deaths* in less than 24 hours were wholly attributed to anaesthesia. In contrast to this 10 of 16 patients still in coma at the end of 24 hours were regarded as being wholly the result of anaesthesia.[5] No data were apparent about how many survived with permanent cerebral sequelae.

Until there are systematic data about brain damaged survivors after medical interventions the best evidence available are the files of the societies that defend doctors against claims for damages. Studies from two UK societies[6,7] and from two American companies[8,9] each indicate a substantial incidence of claims for severe brain damage. Of major claims against anaesthetists 20–40% were for brain damage and the remainder for death. Analysis of all claims for brain damage (excluding infants) showed that 70% had been associated with anaesthesia, including regional and spinal; only 36% of these patients had had a cardiac arrest. One UK society had more than one case of severe cerebral damage following anaesthesia reported each month in the 13 years from 1970 to 1982, with some evidence that the rate was increasing.[6] The UK societies include dentists and also substantial membership in Australasia, which makes it difficult to ascertain the frequency of this problem in medical practice in Britain.

Apart from the causation of severe brain damage anaesthetists are also often involved in the resuscitation and subsequent intensive care of patients who have suffered acute brain damage in other ways. How long to persist with life-sustaining measures is an important and difficult decision. The studies of nontraumatic and of traumatic coma, as well as several others dealing with cardiac arrest, have produced prognostic indices that can identify within a few days whether or not patients are likely to make a reasonable recovery. In such instances steps to withdraw support in order to avoid vegetative survival might be considered. Once the first few weeks have been survived the problem becomes more difficult. In the United States a consensus is emerging that it is appropriate to let such long-term survivors die by withdrawing food and water, and such management has been approved prospectively for several individual patients whose cases have been taken to the courts for a decision.[10] Lengthy discussion of such an approach in a British newspaper provoked no protest.[11]

In the United States there is also increasing concern that doctors should discover what preferences their patients have about the use of life-extending technologies, including the initiation of cardiopulmonary resuscitation, and the continuation

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of life-sustaining measures if rapid recovery does not result. These preferences may be encoded in an advance directive (living will or durable power of attorney) or they may be determined by asking, when they are admitted to hospital, all patients who are considered likely to be at risk of possibly needing such rescue. In the US this would now include all patients submitting to surgery and general anaesthesia, and the possibility of vegetative survival might even be explicitly stated. While such formalities are not yet common in Britain there is increasing concern about these matters.[10–12] It is becoming accepted that doctors should inform patients more fully about the pros and cons of alternative types of management, and this should include the possibility of adverse outcomes other than death.

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Editorial notices

Anaesthesia News

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Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1988, Volume 43, pages 923–926

Adult respiratory distress syndrome—how many cases in the UK?

N. R. WEBSTER, A. T. COHEN AND J. F. NUNN

Summary

Previously reported figures for the incidence of Adult Respiratory Distress Syndrome, based largely on American results, would suggest that the average British Health District of 200 000 people could expect to see 130 cases per year. This figure is greatly in excess of that expected from our clinical experience. We have undertaken a retrospective survey of patients within a British Health Region (population, 3 599 400). Results indicate an incidence of nine for an average Health District of 200 000 population, or 2.5% of all admissions to intensive therapy units, or 0.045 per 1000 resident population.

Key words

Lung; adult respiratory distress syndrome.
Statistics; incidence.

The adult respiratory distress syndrome (ARDS) was described first by Ashbaugh and his colleagues in 1967[1] and since that date has remained a dominant problem of intensive care units because of its frequency, relentless progress and high mortality. The clinical and histopathological picture is remarkably consistent, but the aetiology is multifactorial[2] and prediction of its onset in any individual patient is notoriously difficult. Specific therapy remains elusive but the cost of supportive therapy and the mortality both continue to be distressingly high.

Surprisingly, there has been no estimate of the incidence of ARDS in this country and very little from other countries. The much quoted American Lung Program of 1972[3] estimated the incidence in the USA to be 150 000 cases per year, which would correspond to 130 per year in a typical British Health District which serves a population of 200 000. It should be emphasised that the figure for the incidence in America is an estimate (said in the report[3] to be 'a conservative estimate'), and is not backed by data to support it. Bauman *et al.*[4] determined the incidence of and mortality from ARDS in a large metropolitan medical centre in the USA. A total of 11 112 patients who were considered at risk of developing ARDS were seen in the hospital receiving room during 1983. Ninety-six of these patients subsequently developed ARDS. Both of these American studies produce an incidence of ARDS greatly in excess of that which we would have expected from our clinical experience.

We have therefore undertaken a retrospective survey of the number of patients who develop ARDS in intensive therapy units (ITU) in a single British Regional Health Authority in an attempt to provide some assessment of the incidence of ARDS in the UK.

Methods

One Regional Health Authority (Yorkshire) was selected for study. There is little Regional cross-boundary flow of patients because all medical and surgical specialties are served within the Region. Individual contacts were made with the consultant in charge of every ITU (data obtained from the Intensive Care Society year book). Each was then sent a copy of a questionnaire (Appendix) that relates to all admissions to the unit from 1 January–31 December 1985. Some of the questions allowed open responses so that an idea could also be gained of the diagnostic criteria and current therapy applied throughout the region. Included with the questionnaire was a list of what the authors considered to be causally related factors associated with ARDS[5] (Table 1). Respondents were free to comment on this list.

Figures for resident population were obtained from the Office of Population Censuses and Surveys (OPCS). These data relate to a mid-1985 estimate of the Yorkshire Regional Health Authority resident population.[6] Statistical analysis was performed using the Chi-squared test with Yates' correction; a value of $p < 0.05$ was taken to indicate statistical significance.

N.R. Webster, BSc, MB, ChB, PhD, FFARCS, Member of Scientific Staff, J.F. Nunn, MD, PhD, FRCS, FFARCS, FFARACS(Hon), FFARCSI(Hon), Head, Division of Anaesthesia, Clinical Research Centre, Watford Road, Harrow, A.T. Cohen, MB, ChB, FFARCS, Consultant, Department of Anaesthesia, St James's University Hospital, Beckett Street, Leeds.
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Table 1. Conditions associated with ARDS. Adapted from Fein *et al.*[5]

Presumed direct injury	Presumed indirect injury
Thoracic trauma	Systemic sepsis
Contusion	
Aspiration	Shock of any cause
Gastric juice	Nonthoracic trauma
Drowning	Drugs
Hydrocarbon	Heroin, methadone
Inhaled toxins	Aspirin, barbiturates
Smoke	Blood transfusions
Corrosive chemicals	Pancreatitis
Infection	Severe neurological injury
Viral, bacterial	Post-cardiopulmonary bypass
Miliary TB	Diabetic ketoacidosis
Legionella	
Emboli	
Amniotic fluid embolus	
Fat emboli	
Lymphangiogram	
Radiation	
Drugs	
Paraquat	
Bleomycin	

Results

The response rate was 88% and results were available from 15 of the 17 intensive therapy units in 14 of the 17 Health Districts in the Yorkshire Region; these accounted for 3 102 500 persons, or 86% of the resident population of the region (3 599 400). The admission rate to intensive therapy units during 1985 was 1.82/1000 resident population (Table 2). Two and a half percent of these patients developed ARDS (0.045/1000 resident population), with a mortality of 38%. Approximately 15–20% of ITU admissions throughout the region belonged to one of the causally related groups associated with ARDS. Approximately 14% of these patients subsequently developed ARDS.

Table 2. ITU admissions, incidence and mortality of ARDS. One District had more than one ITU and thus accounted for a total of 15 questionnaires returned. The table excludes one District without an ITU and two Districts from which information was not available.

District	Resident population × 1000	Admissions to ITU	% at risk	Cases of ARDS	Deaths from ARDS
1	159.7	300	< 10	4	2
2	193.4	156	10–20	11	5
3	259.3	363	41–50	6	3
4	142.6	134	10–20	1	1
5	133.9	199	< 10	0	0
6	338.8	227	51–60	41	4
7	172.9	1132	< 10	0	0
8	191.7	231	< 10	9	2
9	212.5	650	10–20	10	4
10	166.4	36	10–20	1	0
11	350.4	1198	21–30	34	21
12	360.1	659	< 10	10	5
13	142.2	345	61–70	10	5
14	112.6	15	31–40	2	1
Total	3102.5	5636		139	53

All units used the characteristic chest X ray picture to help diagnose ARDS. Units were in general agreement about the level of hypoxaemia which would be expected to be associated with ARDS (Fig. 1) and most used a figure for arterial oxygen tension ($Pa\text{O}_2$) of less than 8 kPa at a fractional inspired oxygen tension ($F\text{IO}_2$) of 0.5 (range $Pa\text{O}_2$ 7–8 kPa at $F\text{IO}_2$ of 0.4–0.6). Most units did not measure pulmonary capillary wedge pressure (PCWP) or static lung compliance. Persons responding to the questionnaire were in broad agreement with the causally related groups suggested by Fein *et al.*[5]

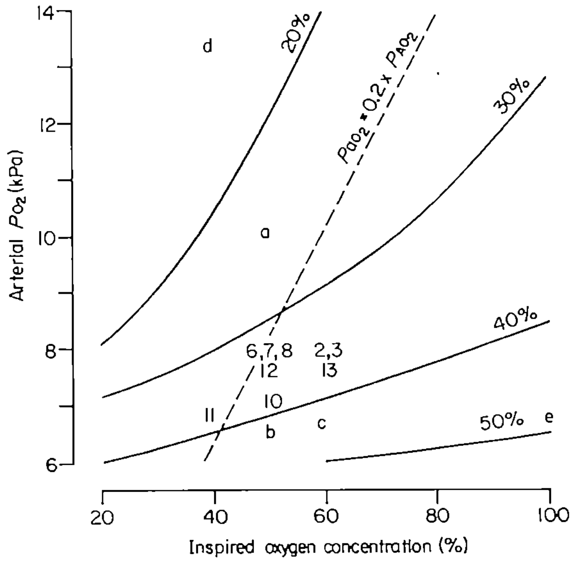

Fig. 1. $Pa\text{O}_2$ as a function of $F\text{IO}_2$ with iso-shunt lines of 20–50% overlaid. The dashed line corresponds to the hypoxaemia criterion suggested by Fowler *et al.*[12] (assuming normal $P\text{CO}_2$). Other workers' criteria of hypoxaemia are shown as individual points: (a) Pepe *et al.*[2] (b) Baumann *et al.*[4] (c) Petty and Fowler,[7] Fein *et al.*[8] and Rosenthal *et al.*[9] (d) Weigelt *et al.*[10] (e) entry criteria for extracorporeal membrane oxygenation (Zapol *et al.*[11]). Hypoxaemia criteria for each individual District are shown as numerals (Table 2).

All responding units were prepared to use positive end expiratory pressure (PEEP) of up to 1.5 kPa in ventilated patients with ARDS. None, however, used higher levels of PEEP as has been suggested in some series.[13] Six units were using high doses of steroids routinely in patients who were considered likely to develop ARDS (Table 3). Sixty-four cases from 2286 admissions (2.8%) were seen in the units which used steroids compared with 75 from 3350 admissions (2.2%) in the units which did not. Mortality in ARDS patients was higher ($p < 0.001$) in the units that did not use steroids (40; 53%) than in the units that did (12; 19%).

Table 3. The use of high dose steroids in patients at risk of developing ARDS and its effect on mortality.

	High dose steroids	
	Used	Not used
Number of ITUs	6	9
Number of ITU admissions	2286	3350
Patients who developed ARDS	64	75
Number who died with ARDS	12	40*

* $p < 0.001$.

Discussion

A recent editorial[14] and review from this country by Wardle[15] have stressed how common ARDS is in Britain. The results of our survey of the incidence of ARDS in the Yorkshire Region in 1985 are at variance with both the Report of the American Lung Program of 1972[3] and Wardle's review. The former predicted an annual incidence of 0.63/1000 and the latter 0.2–0.3/1000. We found 0.045/1000. This is equivalent to about nine cases a year in an average District of 200 000 instead of 130 as predicted from the Report of the American Lung Program, or 40–60 cases as suggested by Wardle.[15] Approximately 1000 of the admissions were thought to be at risk of developing ARDS and 14% of these patients did so. This figure is similar to that obtained by Fowler *et al.*[12] who studied patients admitted to three hospitals in Denver.

A major problem in comparison of incidence and mortality of ARDS between different centres is the lack of any standardisation of diagnostic criteria, particularly in the important field of arterial hypoxaemia. Critical levels of hypoxaemia have been defined by many different combinations of $Pa\text{O}_2$ and $F\text{IO}_2$. These are compared best in terms of the iso-shunt diagram (Fig. 1), because there is evidence that, to a first approximation and in the short term, $Pa\text{O}_2$ changes in response to changes in inspired oxygen concentration as though the venous admixture (shunt) in the lung was constant.[16] Published criteria for ARDS include combinations of $F\text{IO}_2$ and $Pa\text{O}_2$ that correspond to shunts of 15–50%, although there is some indication of a growing consensus view for 40%. An alternative approach is to define critical hypoxaemia as $Pa\text{O}_2$ which is less than 20% of the alveolar $P\text{O}_2$.[12] The broken line in Fig. 1 shows that this cuts across iso-shunt lines from 25–50% and, for a patient with a constant shunt, the ratio tends to decrease as the inspired oxygen is increased and gives a false impression of deterioration. The hospitals reviewed in this study were reasonably consistent in their criteria for hypoxaemia but, even in this small series, the mortality was highest for the hospitals whose criteria corresponded to the largest shunts.

There is widespread agreement that bilateral widespread infiltrates in the chest radiograph constitute a cardinal feature of ARDS. Pulmonary wedge pressure should remain normal in ARDS without left ventricular failure but this was determined in only two hospitals (11 and 12).

We suggest that the following criteria should be used: bilateral widespread infiltrates on chest X ray (although some cases of pulmonary oedema that result from increased alveolar-capillary permeability may be unilateral); $Pa\text{O}_2 < 8$ kPa when inspiring oxygen at $F\text{IO}_2 > 0.5$; PCWP < 15 mmHg if available (not mandatory); and total static compliance <500 ml/kPa.

Accurate record keeping of patients who are discharged from or die in the ICU is of major importance. No quantitative or qualitative comparison can be made between ITUs without such data and no evaluation made of cost-effectiveness. Most units in our survey could provide accurate figures for admissions. However, most did not have accurate data of patients who developed ARDS because of the lack of universally accepted diagnostic criteria and the fact that ARDS is not separately recorded in the Intensive Care Society annual statistics. As would be expected ARDS incidence in ITU patients was higher in Districts that act as Regional referral centres than in other Health Districts. Consequently, most cases were seen in the Leeds and Bradford Districts.

The lower mortality from ARDS in hospitals which use steroids routinely was surprising. However, the use of high-dose steroids made no difference to the number of ITU patients who developed ARDS. Recent prospective studies have demonstrated that the use of steroids in susceptible patients does not alter either ARDS incidence[17] or mortality.[18] All units concerned were using similar diagnostic criteria to distinguish ARDS so that this difference is unlikely to be from the inclusion of inappropriate patients in some centres. It is possible, however, that differences in the presenting pathologies between units may account for the apparent beneficial effect associated with steroid usage.

Results were not available from two Districts in the Yorkshire Region. These two Districts are adjacent and contain all of the major surgical specialties. Consequently, they would not be expected to have many cross-border referrals into other Yorkshire Health Districts and we believe that no appreciable error has been introduced by the exclusion of these two Districts. One further District had no ITU. All data refer to the remaining 14 Districts.

The difference in incidence of ARDS in our series compared with the published figures from America has to be explained. It is possible that our results are falsely low as a result of patients with ARDS who remain undiagnosed or a reluctance of the attending physician to diagnose ARDS because of feelings of personal failure. It may be, however, that the American figures are falsely high as a result of inclusion of patients with either pulmonary oedema not due to increased alveolar capillary permeability, or pneumonia. Another factor to explain the apparent difference in incidence is the failure to standardise criteria of hypoxaemia. However, probably the major factor is that our study is the first and only one which attempts to define the incidence of ARDS in all institutions within a defined and large population base.

The incidence can be determined with greater precision by a prospective study using standardised entry criteria. Such a study would be valuable in view of the results presented, and is now in progress.

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Appendix

1. How many patients with ARDS have you had on your ITU from 1 January 1985–31 December 1985? ☐☐
2. Total number of admissions to your ITU from 1 January 1985–31 December 1985? ☐☐☐☐
3. What % of these ITU admissions do you estimate were at risk (i.e. belonging to causally related groups)? ☐
   <10% = 0 50–60 = 5
   10–20 = 1 60–70 = 6
   20–30 = 2 70–80 = 7
   30–40 = 3 80–90 = 8
   40–50 = 4 >90 = 9
4. How many patients in 1 above died? ☐☐
5. What are your diagnostic criteria for ARDS? Please answer YES or NO and fill in figures as appropriate

	Yes	No
i Chest X ray changes	☐	☐
ii $Pa\text{O}_2$ .... at $F\text{IO}_2$ .... or $Pa\text{O}_2/F\text{IO}_2$ ratio	☐	☐
iii Static compliance > .... ml/cm H_2O	☐	☐
iv Pulmonary capillary wedge pressure < .... mmHg	☐	☐

6. Do you routinely use the following in ARDS patients?

	Yes	No
Steroids	☐	☐
PEEP	☐	☐
PEEP > 15 cm H_2O	☐	☐

7. Are the answers to questions 1, 2 and 4 estimates? ☐ ☐

Anaesthesia, 1988, Volume 43, pages 927–929

Anaesthetic induction with isoflurane or halothane

Oxygen saturation during induction with isoflurane or halothane in unpremedicated children

A. J. PHILLIPS, J. R. BRIMACOMBE AND D. L. SIMPSON

Summary

The authors performed a randomised, prospective trial in which one junior anaesthetist administered gaseous induction of anaesthesia to 50 unpremedicated children with either isoflurane or halothane in nitrous oxide and oxygen. Arterial oxygen saturation and the electrocardiogram were monitored and the incidence of complications noted. Desaturation below 85% occurred in six children, but only with isoflurane. The incidences of complications and desaturation events did not alter throughout the 25 isoflurane inductions. Coughing, movement, laryngospasm and sinus tachycardia occurred more frequently with isoflurane. Isoflurane inductions took longer (7.9 as compared with 5.4 minutes, $p < 0.001$) and had 4.25 times the number of complications.

Key words

Anaesthetics, volatile; isoflurane, halothane.
Monitoring; arterial oxygen saturation.

Halothane has long been regarded as the volatile agent of choice for gaseous induction of anaesthesia in children. The recent introduction of isoflurane has provided an alternative agent with the advantages of low blood solubility, stability of cardiac rhythm, and minimal metabolism with a reduced potential for organ toxicity. These advantages may be offset by a tendency to irritate the airway.

Many children who present for general anaesthesia are unpremedicated day cases scheduled to undergo minor surgery, and gaseous induction is an acceptable part of the anaesthetic technique. The present study was designed to compare halothane and isoflurane during induction of anaesthesia in unpremedicated children as administered by a senior house officer with 18 months' nonpaediatric anaesthetic experience.

Methods

Fifty unpremedicated children (aged 2–12 years, ASA 1) who presented for minor daycase surgery under general anaesthesia were allocated randomly to be induced either with halothane or isoflurane in nitrous oxide and oxygen. Children who volunteered a preference for an intravenous induction or had received a general anaesthetic in the previous 6 months were excluded from the trial. Fresh gas flows of oxygen (3 litres/minute) and nitrous oxide (6 litres/minute) were administered through a coaxial (Bain) system by holding a cupped hand over the mouth and nose until the child was sleepy enough to accept a mask. The inspired concentration of volatile agent was increased in a stepwise manner as tolerated clinically to a maximum of 5%; it was reduced subsequently to achieve a clinically satisfactory level of anaesthesia.

All inductions were performed by one anaesthetist with 18 months' nonpaediatric experience and no previous experience of gaseous induction with either agent. Each induction was monitored by senior observers who were unaware of the agent being used. The observer noted the times to onset of regular breathing, airway insertion and attainment of 5% volatile agent. The incidences of coughing, laryngospasm, breath-holding, salivation, vomiting and dysrhythmias were noted and scored according to the scheme shown in Table 1. The endpoint of induction was defined as the time at which regular breathing had been maintained for 2 minutes after the insertion of an oropharyngeal airway and attainment of 5% volatile agent.

Table 1. Scoring system for assessment of severity of complications.

Grade	0	1	2	3
Cough	Absent	$Sao_2 \geqslant 85$	$Sao_2 \geqslant 75$	$Sao_2 < 75$
Laryngospasm	Absent	$Sao_2 \geqslant 85$	$Sao_2 \geqslant 75$	$Sao_2 < 75$
Breath-holding	Absent	$Sao_2 \geqslant 85$	$Sao_2 \geqslant 75$	$Sao_2 < 75$
Movement	Absent	No restraint	Restraint	Abandon
Vomiting	Absent	Present		
Salivation	Absent	Sucker used		

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Table 2. Demographic data of the two groups.

	Isoflurane ($n = 25$)	Halothane ($n = 25$)
Males : Females	3:1	3:1
Age, years, mean (SEM)	6.6 (0.7)	6.6 (0.7)
Weight, kg, mean (SEM)	24.6 (2.0)	24.0 (2.0)

The electrocardiogram was monitored continuously throughout induction and arterial oxygen saturation (Sa_{O_2}) recorded by a pulse oximeter (Nellcor N-100) using a disposable sensor applied to the toe. Sa_{O_2} was recorded automatically every 30 seconds, with additional recordings of any values below 90%. The anaesthetist was unaware of the Sa_{O_2} but was free to alter or abandon the induction technique at any time if indicated clinically. If Sa_{O_2} decreased below 85% the anaesthetist was informed immediately and administered 50% oxygen with continuous positive airway pressure and assisted ventilation if necessary. The induction technique was abandoned if Sa_{O_2} decreased below 75%; the patient was given 100% oxygen and the trachea was intubated, the patient allowed to awaken or an alternative anaesthetic agent was administered, as appropriate.

Data are presented as mean (SEM). Statistical analysis of data was undertaken using the unpaired Student's *t*-test for demographic data and induction times, and the Chi-squared test for oxygen saturation data and incidences of complications.

Results

Demographic data are shown in Table 2. There were no significant differences between the two groups. Twenty-two of the 25 patients in the halothane group maintained $Sa_{O_2} \geqslant 95\%$ compared with only 14 in the isoflurane group ($p < 0.05$; Fig. 1). All patients in the halothane group maintained $Sa_{O_2} \geqslant 85\%$ compared with 19 in the isoflurane group ($p < 0.01$). Cyanosis was noted on three occasions during the study, all in patients in the isoflurane group in whom Sa_{O_2} decreased below 75%.

Halothane administration was associated with significantly fewer airway-related complications than isoflurane (Table 3). The incidences of complications did not decrease as the study progressed. Laryngospasm occurred in only one patient during halothane induction, but in 13 with isoflurane ($p < 0.001$). Coughing occurred on three occasions with halothane and 12 times with isoflurane ($p < 0.01$) and was more severe when isoflurane was used. Movement (all grades) occurred seven times with halothane and 20 times with isoflurane ($p < 0.001$); restraint was required on 12 occasions in patients who received isoflurane.

There was no difference in the incidence of nodal rhythm between the groups, although sinus tachycardia (rate > 150 beats/minute) occurred only in the isoflurane group. Atrioventricular dissociation occurred once with isoflurane. No other dysrhythmias were noted. The mean induction time for halothane was 5.4 (0.2) minutes compared with 7.9 (0.3) minutes for isoflurane (Fig. 2). Vomiting did not occur in either group. Excessive salivation occurred three times with isoflurane, but never with halothane.

Discussion

Halothane, a halogenated hydrocarbon, has been a popular and successful volatile agent in paediatric anaesthesia since

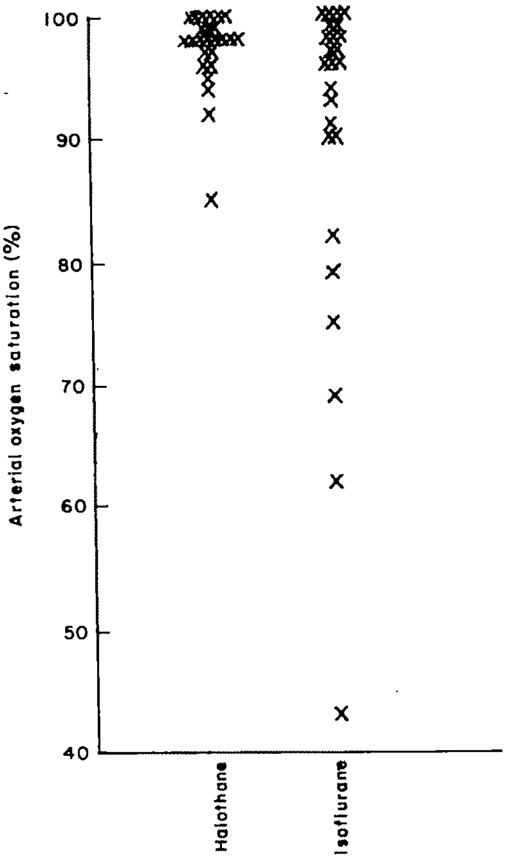

Fig. 1. Minimum arterial oxygen saturations during anaesthetic induction with isoflurane or halothane.

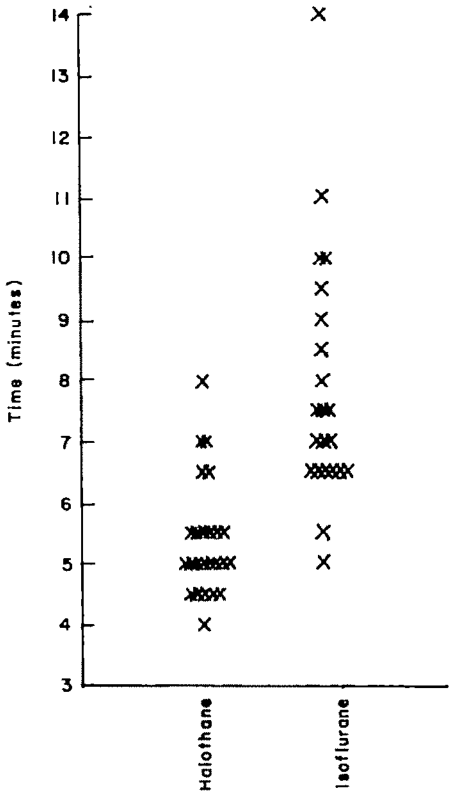

Fig. 2. Duration of anaesthetic induction with isoflurane or halothane.

Table 3. Incidences of complications during induction.

Complication	Grade	Halothane	Isoflurane	p
Cough	0	22	13	<0.01
	1, 2, 3	3	12	
Laryngospasm	0	24	12	<0.001
	1, 2, 3	1	13	
Breath-holding	0	24	22	NS
	1, 2, 3	1	3	
Movement	0	18	5	<0.001
	1, 2, 3	7	20	
Vomiting	0	25	25	NS
	1	0	0	
Salivation	0	25	22	NS
	1	0	3	

its introduction into clinical practice. It allows a smooth and rapid gaseous induction and is well tolerated, but has a tendency to induce cardiac dysrhythmias and undergoes significant metabolism which may lead to a potential for organ toxicity.

Isoflurane, the structural isomer of enflurane, has theoretical advantages in that it induces fewer dysrhythmias and undergoes minimal metabolism. However isoflurane has a pungent, ethereal odour which may cause more airway problems.

Previous studies of isoflurane for gaseous induction in children have varied both in their results and conclusions. Wren *et al.*[1] reported a low incidence of airway problems but used variable premedication in their study of 241 children. McAteer *et al.*[2] confirmed the suitability of isoflurane for gaseous induction, but noted a higher incidence of airway problems, a finding noted also in a number of other studies.[3–5]

One criticism of previous comparative studies is that the anaesthetists have been experienced in the administration of halothane for gaseous induction, but relative novices in the use of isoflurane. The present study was designed specifically to test the hypothesis that there is a 'learning curve' for isoflurane. The anaesthetist was not blinded to the agent being used and was permitted to vary the rate at which the inspired concentration of volatile agent was increased in order to allow improvement in induction techniques with experience.

Induction complications occurred 3.4 times more often with isoflurane and there were higher incidences of movement, laryngospasm and coughing. Arterial desaturation below 85% occurred only in the isoflurane group ($n = 6$) and was associated with airway complications; cyanosis was noted in three of these patients. However airway complications occurred without desaturation in another 13 patients in the isoflurane group. These desaturation incidents were unpredictable, and occurred during the latter half of the induction sequence. Airway complications did not occur less often as the study progressed and experience was gained, even though the inspired concentration of isoflurane was being increased much more slowly in the latter half of the study. The fact that the incidence of complications was so low in the halothane group suggests that difficulty with the technique of gaseous induction *per se* was not a significant factor. Our finding that isoflurane inductions were slower, despite the relative insolubility of isoflurane in blood, agrees with previous studies.

We conclude that isoflurane can cause serious, unpredictable decreases in arterial oxygen saturation when used for gaseous induction in children and that these episodes occur despite increasing familiarity with the technique. We suggest that this risk must be considered when an agent is selected for gaseous induction in children.

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Antagonism of neuromuscular blockade

The cardiovascular effects in children of the combination of edrophonium and glycopyrronium

D. R. GOLDHILL, A. PYNE AND C. J. JONES

Summary

Glycopyrronium 5 or 10 µg/kg was administered either simultaneously with, or 1 minute before, edrophonium 1 mg/kg in order to antagonise competitive neuromuscular blockade in 80 children. Both doses of glycopyrronium given before the edrophonium resulted in an initial significant ($p < 0.01$) increase in heart rate. Heart rate decreased significantly ($p < 0.01$) in all groups after the edrophonium was given, and only glycopyrronium 10 µg/kg administered before edrophonium prevented a substantial decrease below baseline. Initial heart rate responses to glycopyrronium or edrophonium are rapid, and measurements at intervals of 30 seconds may be necessary to record these changes.

Key words

Antagonists, neuromuscular relaxants; edrophonium.
Parasympathetic nervous system; glycopyrronium.

Edrophonium, a reversible cholinesterase inhibitor, has been proposed as an alternative to neostigmine for antagonism of non-depolarising neuromuscular blockade in children.[1] Advantages claimed for edrophonium are a faster onset of reversal and fewer muscarinic effects compared with neostigmine.[2] Glycopyrronium has advantages over atropine as an anticholinergic agent to antagonise the muscarinic effects of neostigmine;[3] these advantages include greater stability of heart rate, a lower incidence of dysrhythmias,[3] and faster arousal and return of cognitive function after general anaesthesia.[4–6] The combination of edrophonium and glycopyrronium may therefore have advantages over that of neostigmine and atropine. It is especially useful to prevent bradycardia in children, and the longer duration of glycopyrronium compared with edrophonium may be considered an advantage.

The combination of edrophonium and glycopyrronium has been examined in adults.[7,8] In both these studies the glycopyrronium was administered simultaneously with the edrophonium, and prior injection of glycopyrronium was not investigated. We believed that the optimum combination might involve the administration of glycopyrronium before edrophonium because of the more rapid onset of the effects of edrophonium.

An initial study in adults who received edrophonium 1 mg/kg for reversal[9] showed that glycopyrronium 5 µg/kg administered one minute before the anticholinesterase resulted in the best cardiovascular stability. Children often have faster baseline heart rates (HR) than adults, are commonly premedicated with an anticholinergic agent, and may not react in the same way as adults to drugs that affect the heart. Consequently, we decided to investigate the combination of edrophonium and glycopyrronium in children, with the aim of defining a dose and administration sequence that minimises cardiovascular changes.

Methods

Eighty children who underwent a wide range of surgical procedures were studied after approval from the local ethics committee and informed parental consent (Tables 1 and 2). Premedication was routine for our institution and consisted of an anticholinergic (atropine or hyoscine), and for patients heavier than 7 kg an opioid (pethidine compound injection or papaveretum). Induction was gaseous (cyclopropane or nitrous oxide/halothane), or intravenous (thiopentone). Tracheal intubation was performed after administration of suxamethonium. Anaesthesia was maintained with 66% inspired nitrous oxide and halothane in all but six children in whom isoflurane was substituted for halothane. In addition, 15 children received small doses of fentanyl shortly after induction. Curare was administered to provide neuromuscular blockade. Ventilation was

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Table 1. Median (range) weight, sex, median (range) age, and number under one year for the four groups.

	Weight (kg)	Males : Females	Age (years)	< 1 year
Group 1	11.8	15:5	2.0	6
Glycopyrronium 5 μg/kg, simultaneously	(2.8–39.5)		(3 days–11.1 years)	
Group 2	10.8	12:8	1.9	6
Glycopyrronium 10 μg/kg, simultaneously	(3.4–30.4)		(1 month–8.2 years)	
Group 3	15.1	10:10	3.3	6
Glycopyrronium 5 μg/kg, before	(3.2–26.7)		(3 weeks–7.4 years)	
Group 4	12.7	13:7	2.4	6
Glycopyrronium 10 μg/kg, before	(3.0–46.3)		(1 day–12.2 years)	

Table 2. Mean (SEM) weights and ages of patients younger than and older than one year for the four groups.

	Younger than one year		Older than one year	
	Weight (kg)	Age (years)	Weight (kg)	Age (years)
Group 1	5.2 (0.7)	0.2 (0.1)	16.4 (2.3)	4.1 (0.8)
Group 2	6.8 (1.2)	0.4 (0.1)	17.0 (2.1)	4.2 (0.7)
Group 3	5.3 (0.6)	0.4 (0.1)	18.5 (1.4)	6.3 (1.4)
Group 4	6.0 (1.0)	0.4 (0.1)	18.2 (2.7)	5.2 (1.0)

adjusted to maintain an end-tidal carbon dioxide tension between 4 and 5.3 kPa.

Patients were allocated randomly to one of four groups. All received edrophonium 1 mg/kg administered over 10 seconds at the conclusion of surgery (time 0). In addition, patients in group 1 received glycopyrronium 5 μg/kg simultaneously with edrophonium; group 2, glycopyrronium 10 μg/kg simultaneously with edrophonium; group 3, glycopyrronium 5 μg/kg one minute before edrophonium; group 4, glycopyrronium 10 μg/kg one minute before edrophonium. Glycopyrronium was prepared in two different concentrations and the anaesthetist was unaware which of the two doses was administered. HR and rhythm were recorded continuously from the electrocardiogram (ECG) on to a paper trace until 10 minutes after administration of edrophonium. HR was taken as the average of 10 R–R intervals read from the trace. Arterial pressure (Dinamap) was noted every minute until 10 minutes after reversal, at which time the anaesthetic agents were discontinued. HR was also recorded at 15, 30, 60, and 90 minutes after reversal.

The HR changes within each group were analysed by a repeated measures analysis of variance and by a paired *t*-test. Differences between the groups were analysed using a repeated measures analysis of variance. The approach of Greenhouse and Geisser[10] was used when assessing the significance of the analysis of variance over time.

Results

There were 20 patients in each of the four groups and no statistically significant differences among the groups in respect of age, weight, sex, or ASA status. This was also the case when comparing between groups those children who were younger or older than one year. For clarity of presentation, mean HR during reversal is shown in Table 3, and changes in HR are represented graphically in Fig. 1. There was a significant ($p < 0.01$) dose-related increase in HR from −1 minute to 0 minute when glycopyrronium was administered one minute before edrophonium. HR decreased significantly ($p < 0.01$) at +30 seconds compared to the value at 0 in all groups, and remained different ($p < 0.01$) at +1 minute in every group except group 2 (glycopyrronium 10 μg/kg simultaneously). HR in groups 1 and 3 (glycopyrronium 5 μg/kg either before or with edrophonium) was significantly lower ($p < 0.01$) from +30 seconds to 10 minutes than at −1 minute. HR in groups 1 and 3 differed ($p < 0.01$) from that in groups 2 and 4 (glycopyrronium 10 μg/kg either before or with edrophonium) from 2 minutes onwards. Individual patients in all groups experienced large changes in HR (Fig. 2). Dysrhythmias were observed in nine patients, three each in groups 1 and 3, two in group 4, and one in group 2. All were junctional rhythms and all resolved spontaneously. Systolic arterial pressure remained stable and within normal limits in all groups. The mean baseline HR of patients less than one year old was significantly faster than in those older than one year ($p < 0.01$), but the pattern of change in HR after edrophonium and glycopyrronium was the same for all children. Clinical difficulties that may have been secondary to inadequate antagonism of neuromuscular blockade were seen in one neonate who failed to maintain adequate ventilation postoperatively. His lungs were ventilated overnight and his trachea extubated uneventfully on the following day.

Table 3. Mean (SEM) heart rates (beats/minute) for patients in the four groups, edrophonium given at time 0. Group 1, glycopyrronium 5 μg/kg simultaneously with edrophonium; Group 2, glycopyrronium 10 μg/kg simultaneously with edrophonium; Group 3, glycopyrronium 5 μg/kg one minute before edrophonium; Group 4, glycopyrronium 10 μg/kg one minute before edrophonium.

Time (minutes)	Group 1	Group 2	Group 3	Group 4
−1	131 (8)	126 (8)	127 (8)	126 (8)
−0.5	129 (8)	128 (8)	132 (7)	137 (8)
0	129 (8)	130 (8)	136 (7)	143 (7)
0.5	107 (9)	117 (8)	116 (9)	132 (7)
1	113 (9)	126 (7)	116 (9)	130 (7)
2	116 (8)	132 (6)	117 (9)	135 (7)
3	117 (8)	134 (6)	116 (8)	136 (7)
4	122 (7)	135 (5)	115 (8)	135 (6)
5	122 (7)	135 (5)	115 (8)	137 (7)
6	122 (7)	134 (5)	117 (8)	137 (6)
7	123 (7)	135 (5)	118 (8)	136 (6)
8	122 (7)	136 (4)	117 (7)	135 (6)
9	121 (7)	136 (5)	113 (7)	134 (6)
10	119 (7)	136 (5)	115 (7)	133 (6)
15	128 (7)	136 (4)	126 (5)	131 (6)
30	131 (6)	131 (4)	128 (5)	132 (6)
60	125 (6)	129 (4)	126 (6)	127 (7)
90	127 (5)	123 (4)	127 (7)	128 (7)

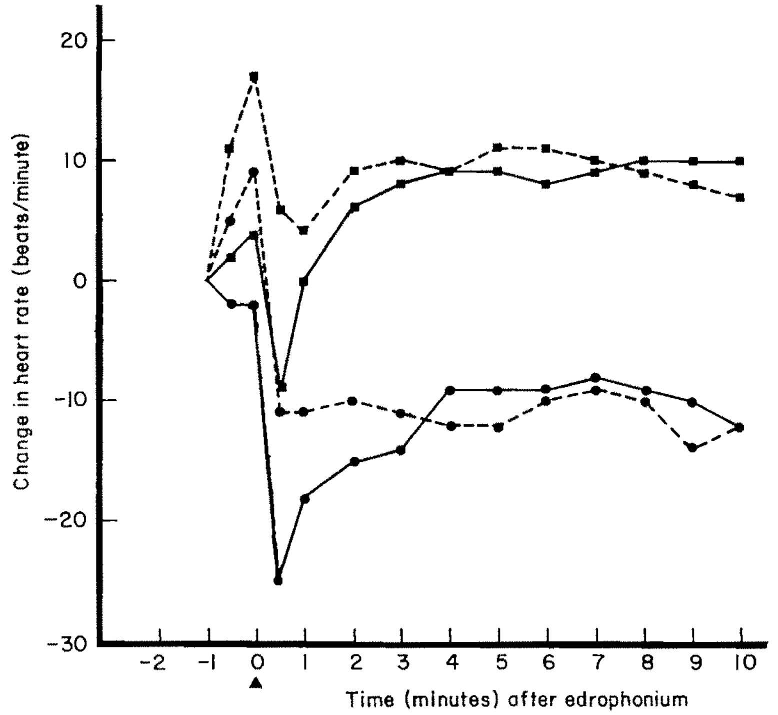

Fig. 1. Changes in heart rate on administration of antagonists. Administration of edrophonium, ▲; glycopyrronium 5 μg/kg, simultaneously with edrophonium, ●——●; glycopyrronium 10 μg/kg, simultaneously with edrophonium, ■——■; glycopyrronium 5 μg/kg, one minute before edrophonium, ●– – –●; glycopyrronium 10 μg/kg, one minute before edrophonium, ■– – –■.

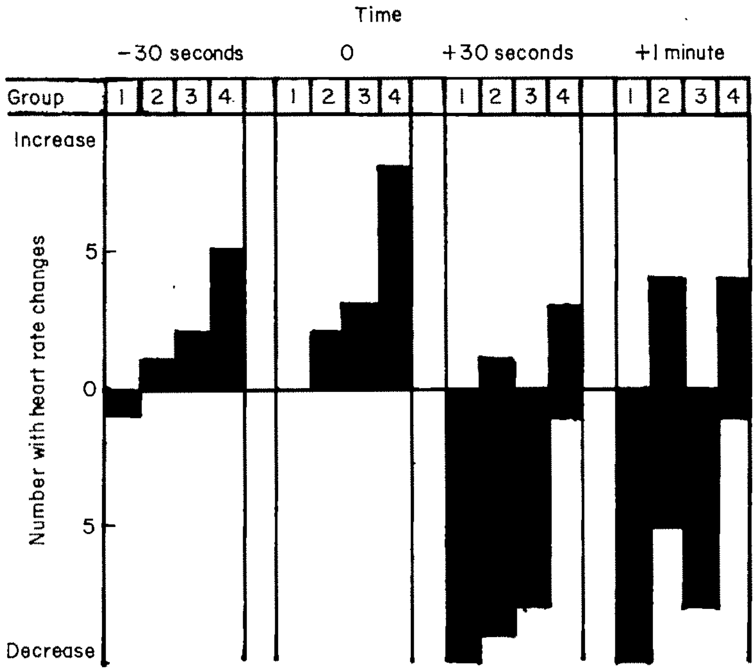

Fig. 2. Number of patients with change in heart rate (HR) of > 15 beats/minute compared with − 1 minute (edrophonium was given at 0). Group 1, glycopyrronium 5 μg/kg simultaneously with edrophonium; group 2, glycopyrronium 10 μg/kg simultaneously with edrophonium; group 3, glycopyrronium 5 μg/kg one minute before edrophonium; group 4, glycopyrronium 10 μg/kg one minute before edrophonium.

Discussion

Studies in adults who received edrophonium for antagonism of neuromuscular blockade have concluded that the simultaneous administration of atropine results in a more stable heart rate than if glycopyrronium is given.[7,8] The combination of edrophonium and glycopyrronium in children has not been reported previously. Simultaneous administration of edrophonium and atropine may result in large variations in heart rate in this age group.[1] The common combination of neostigmine and atropine is associated with cardiovascular instability,[11] and there is evidence that changes in heart rate caused by reversal mixtures may lead in some patients to ischaemic ECG changes and dysrhythmias.[12,13] It is therefore desirable to combine reversal agents in such a way as to minimise cardiovascular changes.

Reversal of profound neuromuscular block may be prolonged irrespective of the choice of anticholinesterase,[14,15] but neostigmine may have advantages over edrophonium.[16] However edrophonium may be superior when used with the medium duration neuromuscular blocking agents because it has a faster onset of action and a greater antifade effect than neostigmine.[17] It has also been suggested that edrophonium may be the antagonist of choice to reverse neuromuscular blockade in patients who have had a bowel anastomosis.[18] Edrophonium 0.5 mg/kg may be appropriate if there has been a moderate degree of spontaneous recovery from the muscle relaxant,[19] but edrophonium 1 mg/kg may be indicated if the block is more profound.[20]

The simultaneous administration of glycopyrronium with edrophonium may produce greater changes in HR than if atropine is given simultaneously with edrophonium, but there may be other reasons for wishing to give glycopyrronium rather than atropine. These include the adverse effect of atropine on postanaesthetic arousal times and memory.[4–6] Glycopyrronium may also provide better control of secretions[11] and has proved, at least when combined with neostigmine, to result in fewer dysrhythmias than atropine.[3]

Previous work in adults given edrophonium 0.5 mg/kg showed that glycopyrronium 5–7 μg/kg administered simultaneously resulted in a transient initial decrease in mean HR and occasional bradycardia in individual patients.[7,8] Glycopyrronium in a dose of 10 μg/kg did not cause an early decrease in HR, but produced a tachycardia from 2 minutes onwards.[7] We obtained similar results with edrophonium 1 mg/kg and glycopyrronium administered simultaneously to adults.[9] However glycopyrronium administered one minute before edrophonium prevented individual episodes of bradycardia, and 5 μg/kg was sufficient for this purpose.[9] Fisher *et al.*[1] found that children required less atropine to prevent bradycardia with edrophonium than with neostigmine. This indicates that edrophonium has relatively less muscarinic effect. However, the authors concluded that atropine should be administered at least 30 seconds before edrophonium to prevent decreases in HR. The decrease in HR was considerable in some individuals given simultaneous edrophonium and atropine, but recovered within one minute of reversal.

In the present study, we have shown that simultaneous administration of glycopyrronium 5 or 10 μg/kg fails to prevent large decreases in HR in some children. Figure 2 shows changes of HR in excess of 15 beats/minute. We realise that this level of change is arbitrary, but the figure is helpful by illustrating the variability of response. Table 4 shows the increase and decrease in HR (if more than 15 beats/minute) in the patient with greatest change in each group. The alterations in HR (more than 50 beats/minute within 30 seconds in some children) were large and sudden enough to cause concern. However none of the patients was given atropine for bradycardia and we had no clinical indication that these brief swings in HR were harmful.

Continuous intra-arterial monitoring was not employed and thus we cannot comment on changes in arterial pressure that may have occurred concurrently with these alterations in HR. Small children are relatively restricted in their ability to alter stroke volume, and cardiac output is dependent largely on changes in HR.[21] It is possible therefore that considerable haemodynamic changes occurred in parallel with the alterations in HR. Most clinicians take great care to maintain cardiovascular stability at induction and during maintenance of anaesthesia. It seems wise to aim for this stability also at the end of the anaesthetic.

Table 4. Increases and decreases in HR (if greater than 15 beats/minute) experienced by patient with greatest change (+, increase; −, decrease) compared with their HR at − 1 minute and at zero time.

− 1 minute

	Time			
	− 30 seconds	0	+ 30 seconds	+ 1 minute
Group 1 +	–	–	–	–
Group 1 −	27	–	53	47
Group 2 +	34	52	42	34
Group 2 −	–	–	35	35
Group 3 +	21	35	–	–
Group 3 −	–	–	49	43
Group 4 +	38	53	42	36
Group 4 −	–	–	18	22

Zero

	Time	
	+ 30 seconds	+ 1 minute
Group 1 +	–	–
Group 1 −	50	45
Group 2 +	–	26
Group 2 −	37	34
Group 3 +	–	–
Group 3 −	46	46
Group 4 +	–	–
Group 4 −	30	35

It is important to note that we could ascertain the changes only by taking initial readings at 30-second intervals. Most notably, if the + 30 seconds reading for group 2 (edrophonium with glycopyrronium 10 μg/kg simultaneously) is omitted, mean HR changes appear to be minimal. Readings at intervals of one minute may disguise large swings within that period. Simply to describe mean HR changes overlooks large alterations that may take place in individual patients. Substantial increases in some patients may balance large decreases in others. An example of this is shown in the results at one minute for group 2 (Figs 1 and 2). The mean HR at this time is no different from baseline, but five patients had a decrease in HR of more than 15 beats/minute relative to the rate at − 1 minute and four children had an increase of the same degree. Glycopyrronium 5 μg/kg given before the edrophonium was also unable to prevent an initial decrease in HR, in contrast to results in adults.[9] Only glycopyrronium 10 μg/kg given one minute before edrophonium prevented large decreases below baseline (HR at − 1 minute), although some children experienced substantial increases in HR with administration of glycopyrronium followed by a decrease towards baseline after edrophonium. HR from 3 minutes onwards remained stable in all groups, although it was greater than the baseline value in groups 2 and 4 (glycopyrronium 10 μg/kg) and lower in groups 1 and 3 (glycopyrronium 5 μg/kg). It is therefore possible that an intermediate dose of glycopyrronium (e.g. 7.5 μg/kg) is optimal and would protect against bradycardia without an increase in HR. Further information on the timing of glycopyrronium with respect to edrophonium would be useful and a shorter interval between the administration of glycopyrronium and the injection of edrophonium (perhaps 30 seconds or less) might decrease the initial tachycardia and thus result in greater cardiovascular stability.

In conclusion, the response to a combination of edrophonium and glycopyrronium appears to be different in children from that in adults. Glycopyrronium 5 μg/kg administered either before or simultaneously with edrophonium 1 mg/kg is insufficient to prevent bradycardia in spite of premedication with an anticholinergic. Simultaneous administration of glycopyrronium 10 μg/kg with edrophonium results in a transient decrease in mean HR which recovers within one minute. Glycopyrronium 10 μg/kg administered one minute before edrophonium prevented bradycardia but resulted in large individual swings in HR.

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Anaesthesia and angiotensin-converting enzyme inhibitors

The effect of enalapril on peri-operative cardiovascular stability

A. P. YATES AND D. N. HUNTER

Summary

The effect of enalapril pretreatment on the haemodynamic response to tracheal intubation and surgical stimulation has been studied in 22 patients. Enalapril 5 mg given 4 hours before operation was associated with a significant reduction in the pressor response associated with intubation ($p < 0.05$) and surgical stimulation ($p < 0.005$) compared with control. Heart rate changes were similar in the two groups. The role of the renin-angiotensin system in relation to the pressor response to sympathetic stimulation is discussed and it is concluded that angiotensin-converting enzyme inhibitors may help improve peri-operative cardiovascular stabiity.

Key words

Pharmacology; angiotensin converting enzyme, enalapril.
Blood pressure; hypertension.

The renin-angiotensin (RA) system plays an important role in the regulation of cardiovascular and fluid-electrolyte homeostasis[1] and is particularly important in the control of blood pressure. Recent evidence has suggested that local RA systems exist at tissue level and may be important in the control of vascular resistance and cardiac and adrenal function.[2]

The effectiveness of angiotensin-converting enzyme (ACE) inhibitors in the treatment of hypertension (essential,[3,4] renovascular[5] or severe accelerated-phase)[6] and afterload reduction in the treatment of heart failure[7] has been well shown. They have been considered the first-step treatment of established essential hypertension in the majority of patients in whom an elevated systemic vascular resistance is the haemodynamic manifestation.[8] The pharmacological properties demonstrated by these agents may be particularly advantageous during anaesthesia and surgery in the control of the haemodynamic response to stress. We have studied the effect of enalapril premedication on the attenuation of the cardiovascular response to laryngoscopy and subsequent peri-operative stability in patients undergoing elective gynaecological surgery.

Methods

Informed consent to a protocol approved by the hospital ethics committee was obtained from 22 patients (ASA class 1 or 2) scheduled for total abdominal hysterectomy. Patients with past or current diagnosis of hypertension or renal disease were excluded as was any patient whose weight was greater than 20% above ideal body weight.

Patients were allocated randomly in a double blind fashion to receive enalapril 5 mg or placebo orally 4 hours before surgery. Premedication with papaveretum 0.3 mg/kg and hyoscine 0.006 mg/kg was given intramuscularly one hour before induction of anaesthesia. Systolic, diastolic, mean arterial pressure (MAP) and heart rate (HR) were measured with an automated blood pressure monitor on admission to the ward, before oral and intramuscular premedication and at one-minute intervals on arrival in the anaesthetic room, where continuous ECG monitoring was also established.

Anaesthesia was induced intravenously in all patients with fentanyl 3 μg/kg given over 30 seconds, followed by thiopentone 4 mg/kg given over 30 seconds and vecuronium 0.1 mg/kg given over 5 seconds. Ventilation of the lungs was then controlled to normocapnia with 50% nitrous oxide in oxygen. Tracheal intubation was performed exactly 4 minutes after the injection of vecuronium when there was no recordable first twitch of a train-of-four. No patient required more than one attempt at intubation. Observations were carried out at one-minute intervals for 12 minutes after the start of the fentanyl injection, at which time the nitrous oxide concentration was increased to 66% and halothane 0.5% was introduced. Normocapnic ventilation was then continued for 20 minutes before the next set of observations (pre-incision) which were recorded at 5-minute intervals thereafter. Compound sodium lactate

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Table 1. Mean values (SD) of age, weight, mean arterial pressure and heart rate for patients who received enalapril (5 mg) or placebo before induction.

	Enalapril ($n = 9$)	Placebo ($n = 13$)
Age, years	40 (5)	47 (8)
Weight, kg	62 (8)	61 (10)
MAP, on admission	88 (13)	85 (13)
before induction	83 (13)	86 (17)
HR, on admission	78 (11)	75 (7)
before induction	75 (15)	71 (18)

solution was infused at a rate of 10 ml/kg/hour throughout the procedure; additional muscle relaxation was given as indicated.

Results

Data were expressed as mean (SD) and analysed by Student's *t*-test ($p < 0.05$ was considered significant). No significant difference existed between the two groups with respect to age, weight, MAP or HR before induction (Table 1). The decrease in MAP and increase in HR was similar in both groups after induction. One minute after intubation the MAP was significantly lower ($p < 0.05$, Fig. 1) in those patients who had received enalapril [MAP = 85(10) mmHg] compared with the placebo group [MAP = 98(18) mmHg]. Changes in HR were similar in both groups. The MAP however, remained lower in the enalapril group for 6 minutes after intubation.

No difference was observed in MAP or HR between the groups immediately before incision (Fig. 2). The MAP was significantly lower 5 minutes after incision in the enalapril group [MAP = 73(10)] compared with those who received placebo [MAP = 96(11)] and for the remainder of the operative period. There was no difference in HR between the groups at any stage during anaesthetic maintenance.

Discussion

Angiotensin II (AII) plays an important role in the regulation of vascular tone and resistance. Local AII concentrations that result from endogenous RA systems based at tissue level may be more important in this respect than those of plasma levels.[2] The reduction of AII levels will not only prevent the direct vasoconstrictor action of the pressor octapeptide but will also inhibit various indirect actions of AII; these include effects on the autonomic nervous system. Angiotensin II increases the prejunctional release of noradrenaline in response to sympathetic nerve stimulation[9] and accordingly ACE inhibition may impair neurogenic vasoconstriction by inhibiting both a prejunctional and postjunctional action of AII.[10]

Inhibitors of ACE are known to reduce blood pressure in normotensives and hypertensives even where patients have normal or low plasma renin activity.[11] Enalapril, the second oral ACE inhibitor, is a prodrug. The active compound enalaprilat is absorbed poorly, hence it is given as the ester which is then hydrolysed to the active drug after absorption. Maximal effect is achieved after 4–6 hours with a duration of 24 hours.

It was seen in our study that enalapril pretreatment resulted in a significant reduction in the pressor responses associated with intubation and surgical stimulation, within the limitations of an automated blood pressure monitor to measure constantly changing haemodynamic variables. No difference was noted in pre- or postinduction, pre-incision MAP or HR between the two groups. A larger dose of narcotic may have achieved the same effect,[12] but would have aggravated respiratory depression. Plasma renin activity, which was not measured in this study, is known to increase in patients who receive ACE inhibitors as a result of loss of feedback inhibition. However, experimental evidence suggests that systemic blood pressure correlates more closely with tissue renin concentrations than with plasma renin activity.[2] Enalapril, unlike many arteriolar vasodilators, does not produce a reflex tachycardia although baroreceptor function appears to be intact. Increased parasympathetic activity has been said to account for this.[13] Beta adrenoreceptor stimulation has been postulated to increase vascular AII production which, in turn, increases catecholamine release from sympathetic nerve endings.[14,15]

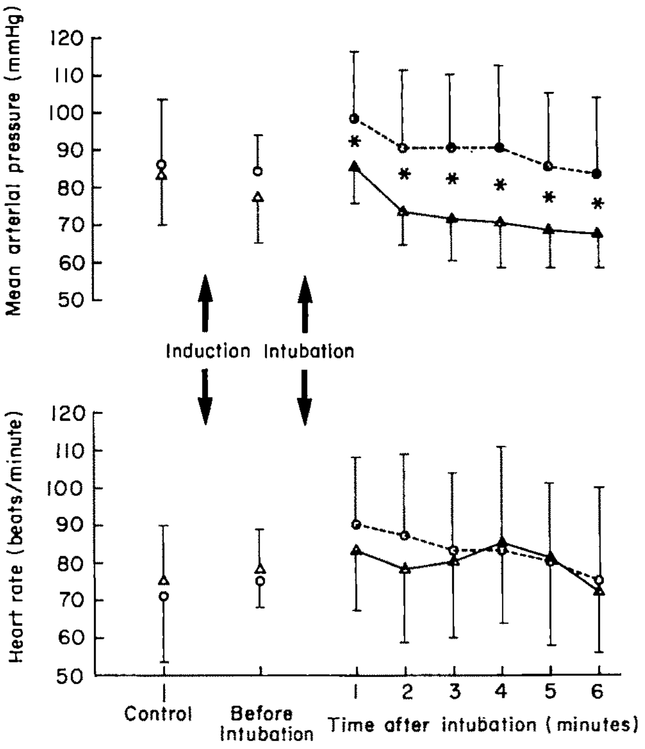

Fig. 1. Mean values (SD) of mean arterial pressure (MAP) and heart rate (HR) before induction of anaesthesia, after induction/before intubation and at one-minute intervals after tracheal intubation for patients who received placebo (—O—) or enalapril 5 mg (—△—) before operation. * Significant differences between groups; $p < 0.05$.

The extent to which the attenuation of the pressor response in this study resulted from the direct or indirect actions of enalapril is unclear. Measurement of circulating catecholamines (which was not performed in this study) has produced conflicting results in hypertensives. Some groups have reported a reduction in plasma noradrenaline[16] but others have not.[17] Interpretation is further complicated by the potential drug interaction between ACE inhibitors and enkephalinase (structurally similar to ACE and responsible for the degradation of enkephalins) which *in vitro* can be inhibited by high doses of ACE inhibitors.[18]

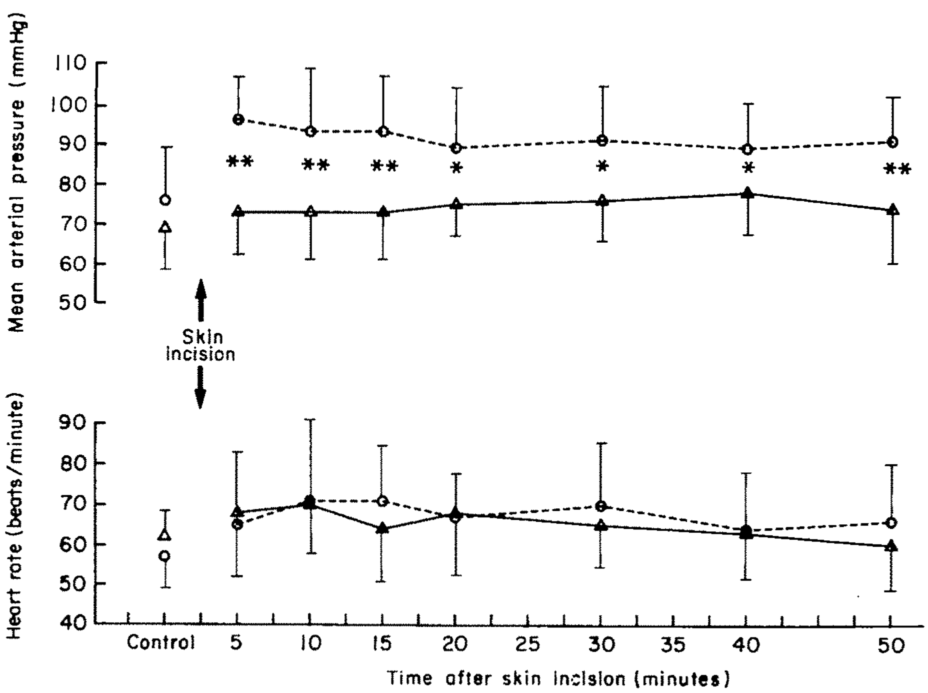

Fig. 2. Mean values (SD) of mean arterial pressure (MAP) and heart rate (HR) before skin incision (control) and at intervals after skin incision for patients who received placebo (--O--) or enalapril 5 mg (—Δ—) before operation. Significant differences between groups; * $p < 0.05$, ** $p < 0.005$.

Inhibitors of ACE have been shown to lower the MAP in normal and hypertensive patients by reducing systemic vascular resistance without changing cardiac output and with slight increase in regional blood flow (cerebral, mesenteric and renal). Coronary blood flow shows little change or a slight decrease appropriate to the decline in myocardial oxygen demand.[19] Use of ACE inhibitors during sodium nitroprusside (SNP) induced hypotension for major orthopaedic surgery has been shown to reduce significantly the dose (and hence potential toxicity) of SNP and attenuate the RA-induced resistance to SNP.[20]

The problem of postoperative hypertension associated with emergence from anaesthesia has been addressed in a recent editorial.[21] The labile heart rate and blood pressure that resulted from increased sympathetic stimulation has important clinical implications particularly in those patients who underwent neurosurgical or major vascular procedures. Pretreatment with ACE inhibitors, which do not exhibit rebound effects on withdrawal, has the potential to improve haemodynamic stability on emergence and may warrant further evaluation. Intra-operative use of ACE inhibitors is, at present, restricted by the lack of an intravenous formulation approved for use. The incidence and severity of adverse effects of ACE inhibitors has been reduced after the realisation that many of the side effects were dose related and could be avoided by the use of smaller doses with little or no loss of efficacy.[22] Circumstances exist however, when particular caution should be exercised. Patients with extreme activation of the RA system can develop dangerous hypotension with the first dose of an ACE inhibitor. Patients at risk are those with severe grades of heart failure or hypertension (especially if diuretic doses are high) or with renal artery stenosis. All patients in the present study were followed up and no adverse effects were seen.

Peri-operative haemodynamic stability and control of sympathetic stimulation are important anaesthetic goals especially in those patients at risk from the complications associated with hypertension and tachycardia. The use of ACE inhibitors in conjunction with general anaesthetics may improve peri-operative cardiovascular stability and warrants further evaluation.

Acknowledgments

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Spread of radiopaque dye in the thoracic epidural space

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Summary

A radiological study was performed in 23 patients to look for the position of thoracic epidural catheters and the spread of the contrast medium iohexol 300 mg/ml and 180 mg/ml when used in volumes of 3 and 8 ml. The dye was injected through the epidural catheter just after thoracic surgery. The spread of the dye showed no relation to the injected volume or the sensory spread after 2% lignocaine 3 ml. In three cases no contrast could be seen on the X ray, and in two the radiopaque dye was found just outside the epidural space. No relationship between the spread of the dye and the sensory blockade was found, but the position of the epidural catheter should be checked radiographically when the epidural route is to be used for long-term pain relief.

Key words

Anaesthetic techniques, regional; epidural.

Epidurography, in 1941, was performed with both air[1] and an ionic water soluble contrast agent;[2] until 1978, only ionic water soluble contrast media were available. Ionic contrast media are known to cause significant injury to the vascular endothelium because of their high osmolarity,[3] and can develop various undesirable effects, especially in the epidural space. Several nonionic iodine containing water soluble contrast media have become available since 1978, which could probably be used epidurally without the side effects associated with the ionic form.

Nowadays epidurography can be used to check epidural catheter position before treatment of pain is started (e.g. postoperative, fractured ribs, inoperable visceral carcinoma, pancreatitis). It was decided to investigate the spread of the contrast in the thoracic epidural space to see if there was any relationship between the spread of the dye and the sensory blockade produced by a test dose of 2% lignocaine 3 ml.

Methods

The study was passed by the hospital ethics committee and informed consent was obtained from each patient. Patients with a history of allergy to iodine or of seizure disorder were not studied. All were scheduled for thoracic surgery.

Epidural catheters were inserted with the patient awake in the sitting position just before surgery. A 16-gauge Tuohy needle was inserted, with a paramedian approach at the T_3–T_4 or T_4–T_5 level. A hanging drop was used to indicate the entry of the point of the needle into the epidural space and confirmed by loss of resistance to air. The catheter was inserted through the needle and directed cephalad 2–3 cm. A bacterial filter was connected and a test dose of 2% lignocaine 3 ml without adrenaline given. The patient was then turned into the supine position and analgesia assessed by response to pinprick 10 minutes after injection of the local anaesthetic. Epidural analgesia was used to supplement general anaesthesia.

Thirteen patients received 3 ml of 300 mg/ml iohexol (Omnipaque 300 R) via the epidural catheter and ten 8 ml of 180 mg/ml iohexol (Omnipaque 180 R) in the recovery room. The volumes 3 ml and 8 ml corresponded with those used for test and therapeutic doses of local anaesthetic respectively. A chest X ray was taken immediately after the injection of the dye. Iohexol is a nonionic highly water soluble radiopaque dye. Viscosity is the same order or a little higher than human blood. The pH is adjusted to 6.8–7.6 with hydrochloric acid.[4]

Results

Analgesia in the segments T_3–$T_{6/7}$ was obtained usually after the test dose of lignocaine (Tables 1 and 2). The epidural position of the catheter tip was confirmed by the appearance of a symmetrical median spread of contrast within the epidural space (Fig. 1). There were no

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Table 1. Demographic data; 3 ml iohexol 300 mg/ml in the thoracic epidural space.

Patient number	Age, years	Sex	Body mass index, kg/sq m	Puncture level	Puncture depth, cm	Spread, local anaesthetic	Spread, contrast medium
1	26	M	18.7	T_4–T_5	7	T_2–T_5	T_1–T_5
2	63	M	23.6	T_3–T_4	7	T_3–T_6	T_2–T_5
3	73	M	25.4	T_3–T_4	5	T_3–T_6	T_1–T_4
4	37	M	21.0	T_4–T_5	6.5	T_3–T_6	T_3–T_5
5	53	M	26.9	T_3–T_4	7.5	T_3–T_6	C_7–T_4
6	57	M	19.8	T_3–T_4	6	T_3–T_6	T_4–T_6
7	20	M	19.9	T_4–T_5	6	T_3–T_6	T_1–T_3
8	60	M	17.2	T_4–T_5	5	T_2–T_5 L T_1–T_7 R	T_1–T_4
9	33	F	19.6	T_4–T_5	6	T_3–T_6	C_5–T_3
10	29	F	22.9	T_3–T_4	7.5	C_7–T_6 L T_3–T_6 R	T_1–T_6

L, Left; R, right.

Table 2. Demographic data; 8 ml iohexol 180 mg/ml in the thoracic epidural space.

Patient number	Age, years	Sex	Body mass index, kg/sq m	Puncture level	Puncture depth, cm	Spread, local anaesthetic	Spread, contrast medium
1	18	M	18.4	T_4–T_5	5.5	T_3–T_6	paravertebral paravascular
2	20	M	22.3	T_4–T_5	6	T_3–T_7	paravertebral
3	16	M	17.9	T_4–T_5	5	nt	T_3–T_6
4	16	M	17.9	T_4–T_5	6	T_3–T_6	C_7–T_{10}
5	60	M	23.4	T_4–T_5	6	T_3–T_6	not visible
6	66	M	30.1	T_4–T_5	7	T_3–T_6L T_3–T_8R	not visible
7	69	M	27.4	T_3–T_4	8	T_4–T_7	T_1–T_3 vague
8	61	M	22.0	T_3–T_4	5	T_3–T_7	T_2–T_6
9	53	M	21.5	T_4–T_5	7.5	T_3–T_7	C_7–T_3
10	18	M	17.4	T_4–T_5	5	T_3–T_6	T_1–T_7
11	41	F	28.7	T_5–T_6	7.5	nt	not visible
12	68	M	20.2	T_4–T_5	7	nt	T_1–T_6
13	51	M	24.8	T_4–T_5	6	T_3–T_6	T_2–T_8

nt, not tested.

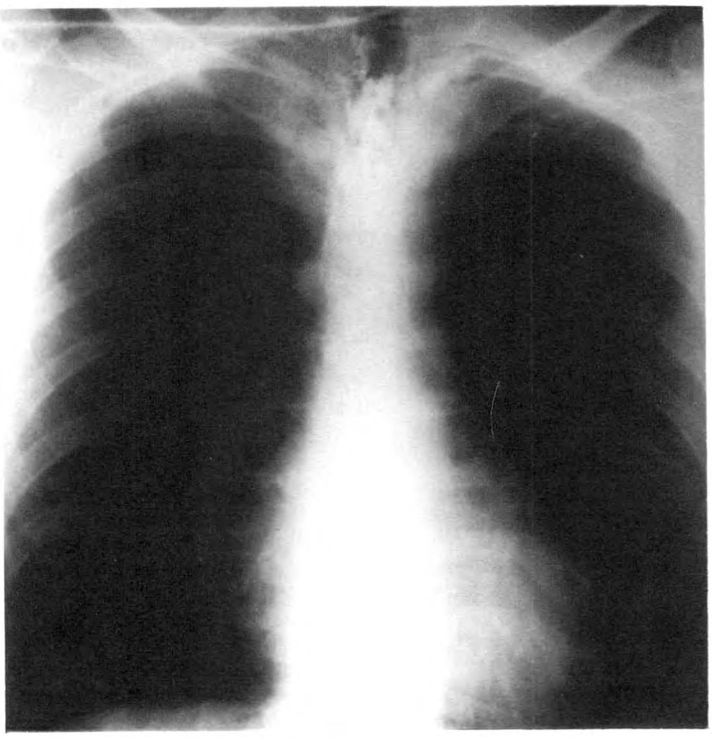

Fig. 1. Chest X ray after 3 ml iohexol 300 mg/ml in the epidural space. A symmetrical spread of contrast in the midline is clearly seen.

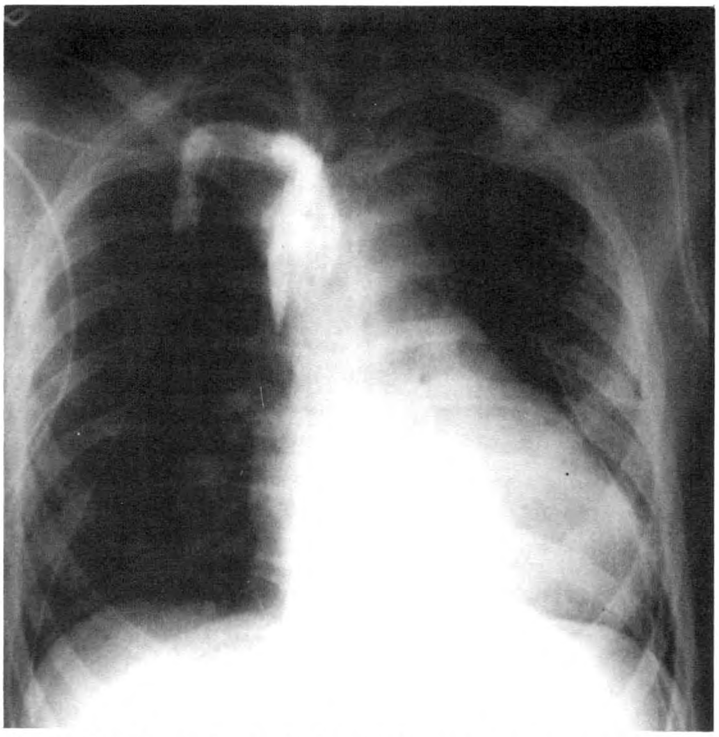

Fig. 2. Chest X ray after 8 ml iohexol 180 mg/ml. Dye is seen in the paravertebral area and there is also some paravascular spread (Patient 1, Table 2).

complications related to the injection of radiopaque dye.

In three patients, all in the high volume low concentration group, the contrast was not visible on the X ray, although excellent pain relief was obtained during and after surgery by injection of local anaesthetic. In two other patients the radiopaque dye was seen just outside the epidural space in the paravertebral area (Fig. 2). In these two patients, (numbers 1 and 2, Table 2), there were some difficulties during insertion of the epidural catheter. In one the catheter could not be advanced more than 1.5 cm and in the other the patient complained of pain during catheter insertion. Segmental analgesia was found after the test dose of lignocaine and the catheter was left in place during surgery. Unfortunately analgesia was not obtained during surgery and both catheters were removed when the chest X ray showed the faulty positions.

Discussion

The introduction of newer nonionic contrast media, with reduced osmolarity and viscosity, make accidental dural or intravenous injection less dangerous.[5,6] Confirmation of epidural catheter position by X ray screening is important if the catheter has to be used for long term pain relief.[7,8] Two inaccurate catheter placements were found in our study, although symmetric sensory blockade resulted after a 3-ml test dose of lignocaine.

Contradictory reports are found in the literature with regard to this subject. Local anaesthetic solutions can reach the epidural space when injected into the intercostal space, as shown by Middaugh *et al.*[9] who used radioactive technetium as a tracer. However in a more recent study[10] paravertebral blocks, neither with large volumes (up to 30 ml of bupivacaine), nor with continuous infusions, resulted in clinical evidence of contralateral blockade. Thus a test dose can be misleading about the real position of the 'epidural' catheter.

Intrathecal diffusion of the local anaesthetic solution could have been responsible for the resulting blockade in the two patients where the contrast was seen in the paravertebral area. Confirmative signs of exact placement of an epidural catheter are painless introduction of the catheter, and introduction without any resistance. Pain or difficulty on insertion are warning signs about the incorrect position.

No contrast could be seen on X ray in three of our cases and a fourth was indistinct (Table 2; numbers 5, 6, 11, and 7). These four patients all had 8 ml iohexol 180 mg/ml. Thus in this clinical setting, with portable bedside X rays, it seems more reliable to choose a more concentrated radiopaque dye. Of course other factors can be responsible for this, such as intravascular injection, obesity, enlargement of the superior mediastinum, or too little contrast medium injected. From the first 10 patients (Table 1), it is clear that the spread of segmental analgesia after 3 ml of local anaesthetic solution is not comparable with the spread of contrast. The initial lignocaine injection and subsequent dye injection were at different times and separated by numerous patient movements, so it is not reasonable to expect such an outcome. Other factors such as viscosity, pH, time of testing the sensory blockade also influence this. Furthermore, the radiopaque dye can only be shown radiologically immediately, as rapid reabsorption occurs.

We conclude that injection of a radiopaque dye of high concentration and low volume through the epidural catheter with subsequent chest X ray gives a better localisation of catheter placement than a test dose of local anaesthetic solution. The majority of thoracic epidural blocks are effective and uneventful, but even in experienced hands inadequate analgesia and unexpected complications remain possible.[7,8] The position of the catheter in these cases can be checked by chest X ray after injection of radiopaque dye. Further indications for radiology are to educate residents, research, injection of neurolytic solutions, and to identify disc herniation.[11,12] The most important contraindications to injection of radiopaque dye are pregnancy, a history of seizure disorder, or allergy to iodine.[13]

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Postoperative recovery after general anaesthesia with and without retrobulbar block in retinal detachment surgery

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Summary

This study was to determine whether general anaesthesia plus retrobulbar block would be a better anaesthetic technique than general anaesthesia alone in retinal detachment surgery. Twenty-eight patients were allocated randomly to either general anaesthesia with retrobulbar block or general anaesthesia alone. The anaesthetist involved was blinded as to whether a retrobulbar block was performed or not. Significantly fewer patients in the general anaesthesia plus block group complained of postoperative pain than patients in the general anaesthesia group (21.4% as compared with 64.3%, $p < 0.05$). Those who received general anaesthesia plus block recovered significantly more rapidly than those receiving general anaesthesia alone. The time to opening of eyes on command ($p < 0.05$), telling the correct date of birth ($p < 0.01$), reaching a full recovery score ($p < 0.005$) and performing a simple motor task ($p < 0.025$) was shorter in patients with general anaesthesia plus block. Thus general anaesthesia plus retrobulbar block was superior to general anaesthesia alone in terms of pain and recovery after operation.

Key words

Anaesthetic technique; nerve block.
Surgery; ophthalmic.

Retinal detachment surgery can be performed safely and conveniently under general anaesthesia. However, we find it is associated with a higher incidence of nausea and vomiting than other ocular procedures performed under general anaesthesia. Retinal detachment surgery is performed satisfactorily under local anaesthesia, but many patients find the experience unacceptable and the quality of akinesia at the start of surgery has been reported as unsatisfactory in 10–20% of patients.[1] We speculated whether a combination of general anaesthesia and retrobulbar block might allow for a reduced dosage of anaesthetic agent intra-operatively while decreasing patient discomfort after operation.

The purpose of this study was to determine whether general anaesthesia plus retrobulbar block in retinal detachment surgery would result in a better anaesthetic technique than general anaesthesia alone.

Methods

Informed consent was obtained from the patients who were to have retinal detachment surgery. All were seen and reassured by their anaesthetists pre-operatively but no premedication was given. They were assigned randomly to have either general anaesthesia plus retrobulbar block or general anaesthesia alone. In the group to have general anaesthesia plus retrobulbar block, 0.5% bupivacaine 4 ml was injected in the muscle cone by the same investigator with a 25-gauge 1.5-inch needle. The retrobulbar block was performed in the anaesthetic induction room before general anaesthesia. Any immediate complications of the block were noted and the eye then covered with a patch. In the group to have general anaesthesia alone, the eye scheduled for operation was also covered with a patch so that the anaesthetist involved would be blinded as to whether a retrobulbar block had been performed.

Anaesthesia was induced with tubocurarine 3 mg, fentanyl 2 μg/kg, sodium thiopentone 4 mg/kg, suxamethonium 1.5 mg/kg all administered intravenously. The patients' tracheas were intubated and ventilation controlled. Anaesthesia was maintained by nitrous oxide, oxygen, tubocurarine, and isoflurane. Intra-operatively, the incidence of bradycardia, defined as heart rate less than 60 beats per minute that occurred during the looping of the rectus muscles, was

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noted. An assessment of pain was made, when the patients arrived in the Post Anaesthetic Care Unit, using a visual analogue scale with a 10-cm line.[2] Patients were asked to indicate their perceived level of pain by marking this line: the left end indicated no pain, and the right end maximum pain. The visual analogue scale was considered to be 0 mm if a patient was asleep or not responding. Nausea, vomiting and pain were registered by the same observer during the first 2 hours after operation. Any incidence of pain, nausea, vomiting and administration of analgesics or antiemetics was registered in the patient's chart by the ward staff.

A scoring system according to Asbury[3] (postanaesthetic recovery score–PARS), which emphasised colour, consciousness, circulation, respiration and movement, was used to assess immediate recovery. The time taken for the score to return to a maximum of 10 was noted, as well as the time patients took to open eyes on command and give correct date of birth. A simple toy shape-sorter was used as a test of postoperative recovery[4] in which a pre-operative value of numbers of shapes posted in 20 seconds was recorded. The same toy test was performed when the patient was sufficiently awake to sit up in bed after operation, and repeated every 10 minutes until they were able to post the pre-operative number of shapes, and the time was noted.

Statistical methods. Student's *t*-test for unpaired differences and Fisher's exact test were used for the statistical calculations.

Results

Patients (Table 1)

Twenty-eight patients completed the study. Fourteen were randomised to have both general anaesthesia and retrobulbar block, while the remainder received general anaesthesia alone (control group). There were no significant differences between the two groups in sex distribution, age, weight, or ASA physical status.

Intra-operative data (Table 2)

Both groups were comparable in mean duration of surgery, duration of anaesthesia, and the amount of analgesics received. In the general anaesthesia plus block group, six out of 14 developed bradycardia whereas in the control group, it occurred in eight out of 14. There was no significant difference in incidence between the two groups.

Postoperative nausea and pain (Table 3)

Nausea and vomiting occurred during the first 2 hours in six out of 14 of the patients (42.9%) who received general anaesthesia alone, wheareas in those with general anaesthesia and block it occurred in only two out of 14 (14.3%). There was a significantly higher incidence of patients who

Table 1. Demographic data.

	General anaesthesia ($n = 14$)	General anaesthesia plus retrobulbar block ($n = 14$)
Males/females	9/5	7/7
Age, years (SD)	59.2 (7.7)	62.4 (13.9)
Weight, kg (SD)	65.7 (17.1)	75.0 (8.9)
ASA class 1	4	4
2	8	9
3	2	1

Table 2. Intra-operative data.

	General anaesthesia ($n = 14$)	General anaesthesia plus retrobulbar block ($n = 14$)
Bradycardia	8	6
Duration of surgery, minutes (SD)	100 (29.8)	99.4 (27.7)
Intra-operative fentanyl, μg (SD)	120 (34.0)	134 (38.0)

Table 3. Nausea and pain after operation.

	General anaesthesia ($n = 14$)	General anaesthesia plus retrobulbar block ($n = 14$)
Nausea and vomiting, first 2 hours	6	2
Nausea and vomiting, 2–24 hours	7	9
Pain, first 2 hours	9	3 ($p < 0.05$)
Pain, 2–24 hours	5	5
Time to first dose of analgesic, minutes (SD)	122.5 (90.4)	732.22 (542.4) ($p < 0.01$)
Requirement of first 24-hour codeine, mg (SD)	103 (56.2)	73.33 (50.0)

Table 4. Recovery after operation. Values expressed as mean (SD).

	General anaesthesia ($n = 14$)	General anaesthesia plus retrobulbar block ($n = 14$)
Time to opening of eyes, minutes	10.8 (8.5)	5.92 (4.8) ($p < 0.05$)
Time to correct date of birth, minutes	15.9 (11.4)	7.17 (5.3) ($p < 0.01$)
Time to full score of PARS, minutes*	88.1 (47.5)	36.07 (50.6) ($p < 0.005$)
Time to control shapes, minutes	111.9 (22.8)	86.45 (28.5) ($p < 0.025$)

* Postanaesthetic recovery score.

complained of pain (nine out of 14, 64.3%) in the control group in the first 2 hours than in the group with retrobulbar block (three out of 14, 21.4%, $p < 0.05$). This difference was reduced in the next 24 hours. The time to first dose of analgesic is significantly longer in the group with block than with general anaesthesia alone [732.22 (SD) 542.4 minute as compared with 122.5 (SD) 90.4 minute, $p < 0.01$]. However, the total amount of codeine required during the first 24 hours after operation is not significantly different between the two groups [73.33(SD) 50.0 mg with block versus 103 (SD) 56.2 mg, without block].

Postoperative recovery (Table 4)

The patients who received the block recovered significantly faster than the control group. Postoperatively, the time to opening of eyes on command ($p < 0.05$) and to telling the correct date of birth ($p < 0.01$) was shorter in the group with retrobulbar block than in the control group. The patients with general anaesthesia plus block reached a full score of PARS in less time than the patients who had general anaesthesia alone ($p < 0.005$). The patients without block also required a longer time to attain control-time in the 'toy test' compared with the group with the block ($p < 0.025$).

Discussion

Most ophthalmic surgery, such as cataract extraction, can be performed under neuroleptic anaesthesia with retrobulbar and facial nerve block. However, there are certain patients who will always require general anaesthesia for a variety of reasons. This study compared two anaesthetic techniques for retinal detachment surgery, general anaesthesia plus retrobulbar block as compared with general anaesthesia alone.

During the postoperative period, general anaesthesia with retrobulbar block was superior to general anaesthesia alone. Significantly fewer patients in the general anaesthesia plus block group complained of postoperative pain than patients in the general anaesthesia group (21.4% versus 64.3%, $p < 0.05$). The time to first dose of analgesic was significantly longer in the group with block than with general anaesthesia alone [732.22 (SD) 542.43 minute as compared with 122.5 (SD) 90.4 minute, $p < 0.01$]. Nausea and vomiting occurred in 42.9% of patients who had general anaesthesia, and 14.3% of patients who had general anaesthesia and retrobulbar block. It was evident, however, that as the effect of the block disappeared, the incidence of pain and nausea became equal in the two groups.

The patients who received general anaesthesia plus block recovered significantly faster than patients receiving general anaesthesia alone. The time to opening of eyes on command, telling the correct date of birth, recovery to a full score of PARS, and psychomotor recovery was shorter in patients with general anaesthesia plus block than general anaesthesia alone. The anaesthetic intravenous induction and maintenance agents were standardised, although the amount of isoflurane required could be different in the two groups resulting in a difference in rate of recovery. However, we were unable to measure the exact level of inhalation anaesthetics employed at the time of our study.

There have been conflicting opinions in the literature with regard to the effectiveness of retrobulbar block in the prevention of oculocardiac reflex. Some have found it effective[5,6] while others have not.[7,8] Retrobulbar block was ineffective in the prevention of bradycardia in our study. We found no side effects or complications from retrobulbar injection of bupivacaine, although there are many potential complications and this additional risk must be considered when adding retrobulbar block to general anaesthesia. Adverse reactions that have been reported include confusion, convulsions, respiratory depression or respiratory arrest, and cardiovascular changes.[9] These reactions are similar to systemic toxicity seen with inadvertent intravascular injection of large doses of local anaesthetics and might be because of intra-arterial or intraneural injection of local anaesthetic with retrograde flow to the cerebral circulation.[10–12] The amount of local anaesthetic necessary for retrobulbar block is small, which minimises the risk of systemic effects, and, in experienced hands, the procedure appears to be safe.

General anaesthesia plus retrobulbar block appears to be an optimal anaesthetic technique for retinal detachment surgery. The postoperative recovery is more rapid and smooth when compared with general anaesthetic alone and may thereby reduce anaesthetic risk, especially in more elderly, high risk patients in whom there is no alternative to general anaesthetic.

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Rectus sheath block for diagnostic laparoscopy

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Summary

Sixty adult females of ASA grade 1 or 2 scheduled to undergo diagnostic laparoscopy were allocated randomly to one of two groups. In group A, laparoscopy was performed with a standardised general anaesthetic technique alone. In group B, the same general anaesthetic technique was supplemented with bilateral rectus sheath block. Postoperative analgesia was assessed at 1, 6 and 10 hours after operation. Visual analogue pain scores in group B were significantly lower than in group A despite a greater use of intramuscular analgesic injections in group A ($p < 0.005$ in each case).

Key words

Pain; postoperative.
Anaesthetic techniques, regional; rectus sheath block.

Laparoscopy is an increasingly popular technique both for diagnostic and therapeutic purposes. The laparoscope is inserted with the aid of a large bore trochar, usually through a midline subumbilical skin incision, to penetrate the rectus sheath and peritoneum. Successful blockade of the relevant intercostal nerves within the rectus sheath should produce full thickness anaesthesia of the anterior abdominal wall, and provide both intra-operative and postoperative analgesia. This study was undertaken to test this hypothesis.

Patients and methods

The study was approved by the District Ethics Committee. Sixty adult females of ASA grade 1 or 2 scheduled for elective diagnostic laparoscopy were studied. The patient was excluded from further study and from the data analysis if surgery was required after laparoscopy. Formal consent to the study was obtained in all cases. Premedication comprised temazepam 20 mg orally, approximately 2 hours before operation. Each patient was allocated to one of the two study groups according to a random number sequence.

Anaesthesia was induced in group A with alfentanil 25 μg/kg body weight and propofol 1.5–3 mg/kg. Vecuronium 0.1 mg/kg was administered both to facilitate tracheal intubation and for intra-operative muscle relaxation. Anaesthesia was maintained with 65% nitrous oxide in oxygen and 0.5% halothane if required. The lungs were ventilated to achieve normocapnia as judged by continuous end-tidal carbon dioxide measurement (Cardiocap, Datex Ltd). Other monitoring included automated oscillotonometry, inspired oxygen concentration, pulse plethysmography and electrocardiography (Cardiocap, Datex Ltd). The pneumoperitoneum (carbon dioxide) was reduced as far as possible at the end of surgery, and neuromuscular blockade was antagonised with neostigmine 50 μg/kg and glycopyrronium 10 μg/kg.

An identical general anaesthetic sequence was used in group B but bilateral rectus sheath block was performed after tracheal intubation. Rectus sheath block was induced by two injections, one on each side of the abdomen. A 22-gauge short bevel needle (Regional block needle, B-D Ltd) was inserted at a point 3–5 cm above the level of the umbilicus at the lateral border of the rectus abdominis. The anterior rectus sheath was identified by moving the needle from side to side whilst advancing the needle until it was felt to scratch the sheath. The needle was then advanced until the resistance of the posterior layer of the rectus sheath was felt. Bupivacaine 0.25% plain was injected in a volume of 0.25 ml/kg (typically 15 ml of solution) after a negative aspiration test.

All patients in the study were prescribed papaveretum 0.3 mg/kg 4-hourly by intramuscular injection as required for postoperative pain relief. The decision to administer papaveretum was at the discretion of the ward nurses, who were blind to the patient grouping. Postoperative analgesia was assessed at 1, 6 and 10 hours after operation by 10-cm visual analogue scores (pain absent = 0, severe pain = 10). The assessment was performed by an observer blind to the patient grouping. Note was made of any administration of intramuscular analgesia.

The data were analysed using the Wilcoxon rank sum

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test, the Chi-squared test (with Yates' correction) or analysis of variance as appropriate.

Results

Six patients were excluded from group A and eight from group B because additional surgery was required; data from 24 patients in group A and 22 in group B were analysed. There were no significant differences between the two groups in respect of age, weight, duration of surgery or individual operator. Analysis of pain scores showed a highly significant difference between the groups at both 1 and 6 hours after operation ($p < 0.005$), and a significant difference at 10 hours postoperatively ($p < 0.05$) (Table 1). The number of patients with a pain score of 0 (pain free) at each assessment is shown in Table 2. The difference between the groups is highly significant at each assessment ($p < 0.001$).

Table 1. Mean (range) pain scores (cm) at each postoperative assessment.

Time (hours)	Group A $n = 24$	Group B $n = 22$	p
1	7.1 (3.1–8.4)	0.7 (0–4.1)	<0.005
6	4.3 (1.6–6.4)	0.4 (0–3.1)	<0.005
10	3.2 (1.4–5.5)	1.6 (0–2.3)	<0.05

Table 2. Number of patients who were pain-free at each postoperative assessment.

Time (hours)	Group A $n = 24$	Group B $n = 22$	p
1	0	19	<0.001
6	0	20	<0.001
10	2	15	<0.001

The number of patients in group A who had received intramuscular analgesia at the 1-, 6- and 10-hour assessments was 17, 18 and 18 respectively; five patients in this group received two doses of papaveretum each. The corresponding figures for group B were 3, 5 and 5, and no patient received more than a single dose. These differences between the groups were highly significant for each of the three assessments ($p < 0.005$ in all cases).

There were no significant differences between the groups in respect of pre-operative or intra-operative heart rates, or mean arterial pressure. The only significant difference between the groups in the postoperative period was for heart rate at one hour; mean heart rate in group A was 97.3 beats/minute (range 84–120), and in group B the corresponding figure was 81.6 beats/minute (64–92) ($p < 0.05$).

Discussion

Both laparascopy and rectus sheath block are surprisingly old techniques (1910 and 1899 respectively).[1,2] Laparoscopy has increased steadily in popularity, but the advent of the neuromuscular blockers in the 1940s led to a rapid decline in the use of local anaesthetic techniques such as rectus sheath block to provide abdominal muscle relaxation. This change in practice meant that the potential for local anaesthesia in provision of postoperative pain relief was largely forgotten. The introduction of local anaesthetic agents with a prolonged duration of action[3] has led to a revival of interest in this facet of local anaesthesia.

The use of rectus sheath block in this study reduced significantly both postoperative pain and the requirement for intramuscular analgesia for at least 10 hours after diagnostic laparoscopy. It remains to be seen whether a similar result would be achieved in patients undergoing laparoscopic procedures such as tubal ablation or occlusion, but initial results in such cases are encouraging (Smith, Allison and Suchak, unpublished observation). Pain after laparoscopy is related not only to the subumbilical entry site; considerable discomfort, particularly shoulder tip pain, may result if gas remains in the peritoneal cavity at the conclusion of the procedure.[4] Carbon dioxide was used as the insufflation gas in this study, and care was taken to reduce residual gas in the peritoneum to a minimum. Only four patients, two in each group, reported shoulder tip pain, but in none of these cases was papaveretum required.

Spread of the local anaesthetic agent in the space between the anterior layer of the rectus sheath and the rectus muscles is restricted by the presence of the tendinous intersections. There are no such intersections between the muscle and the posterior layer of the sheath. The principal determinant of spread is the volume of solution injected if the local anaesthetic agent is deposited in this layer. Advancement of the needle until the point is felt to meet the posterior layer of the rectus sheath ensures that the injection is made at the correct depth, although it should be appreciated that the resistance offered by the posterior rectus sheath is somewhat less obvious than by the anterior layer.

Many anaesthetists perform a crude test of postoperative muscle power by asking the patient to lift the head from the pillow. The weakness of the rectus abdominis that occasionally accompanies a successful rectus sheath block may make this manoeuvre difficult or impossible, and lead to the mistaken diagnosis of inadequate recovery from neuromuscular blockade.

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Induction dose of propofol in children

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Summary

In a study of 144 children aged 1–12 years, attempts were made to assess the ED_{50} and ED_{90} of the intravenous induction agent, propofol. The doses required for loss of eyelash reflex and tolerance of facemask, in 50% of unpremedicated children, were 1.6 mg/kg and 2.5 mg/kg respectively. In children premedicated with oral trimeprazine the corresponding values of ED_{50} were 1.1 mg/kg and 2.0 mg/kg. Doses of 2.8 mg/kg in unpremedicated and 2.0 mg/kg for those who received trimeprazine were required for loss of eyelash reflex in 90% of children. This probably corresponds to an effective induction dose. Pain and movement on induction were common; the incidence was 27% and 21.5% respectively.

Key words

Anaesthetics, intravenous; propofol.
Anaesthesia; paediatric.

Propofol in an emulsion formulation that contains soyabean oil and a purified egg phosphatide has been available for clinical evaluation since July 1983. Pharmacokinetic studies of propofol in adults have demonstrated its high plasma clearance[1–3] and short elimination half-life, which suggests its suitability for daycase anaesthesia. Clinical studies have confirmed rapid postoperative recovery and it appears to be superior to methohexitone[4–6] in this respect. The dose required in adults to induce anaesthesia in 95% of healthy, unpremedicated patients is 2.5 mg/kg.[7] However, there are very few published studies on the use of propofol as an induction agent in children.[8]

The aim of this study was to determine the effective dose of propofol for induction in premedicated and unpremedicated children. Opportunity was taken to make general observations of efficacy and side effects of the drug in this respect.

Method

Forty-six children were used in a pilot study to determine the range of doses which would be appropriate for use in a formal study to detect ED_{50} and ED_{90} (the ED_{50} was taken as that dose which would abolish the eyelash reflex in 50% of the studied subjects). It also became clear from this study that an unacceptably high proportion of children experienced severe pain on injection. Therefore lignocaine was mixed with the propofol for the formal study. The dose used was 2% lignocaine 0.5 ml added to propofol 20 ml, according to the recommendations of Brooker and Redfern.[9] The prepared mixture was used within 25 minutes of preparation.

Informed parental consent and approval from the District Ethics Committee was obtained for both the pilot and definitive studies. In the definitive study 144 mentally normal children in ASA grades 1 and 2 and between 1 and 12 years of age, were evaluated. The study split them into two groups. Group A consisted of 72 children who were premedicated with trimeprazine 3.0 mg/kg up to a maximum of 100 mg. They also received atropine 30 μg/kg orally 2 hours pre-operatively. Group B's 72 children received no premedication. The majority were undergoing surgery as day cases. Both groups had EMLA cream applied over a vein on the dorsum of one hand 2 hours before operation. Each child was allocated randomly to one of the six dose range groups on arrival in the anaesthetic room. These were 1.0, 1.5, 2.0, 2.5, 3.0 and 3.5 mg/kg for the premedicated group A and 1.5, 2.0, 2.5, 3.0, 3.5 and 4.0 mg/kg for the unpremedicated group B.

The allocated dose was administered over approximately 20 seconds through a 25-gauge indwelling needle in the dorsum of the hand. Twenty seconds after the injection two reactions were assessed. Firstly, an attempt was made to elicit the eyelash reflex and if it was lost, the patient was considered a responder. If not, increments of propofol 5–10 mg were given. If no eyelash reflex was elicited, the

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patient's acceptance of a facemask was tested by gently placing an anaesthetic mask over the face and, if necessary, the jaw was lifted to maintain the airway. Nonresponders, evidenced by gross bodily movements, were either given incremental doses of propofol or anaesthesia was deepened with inhalational agents.

Observations were made during this period with regard to apparent pain on injection, erythema and dystonic movements. Postoperatively the nursing staff made routine general observations and noted the presence of any nausea, vomiting and headache. The 50 and 90% effective doses and their confidence limits were calculated using the Fieller macro in Genstat release 4.04B[10] at the University of London Computer Centre. This program fits parallel probit/log dose to the data. The loss of eyelash reflex and the tolerance of facemask were analysed separately. Alternative statistical calculations were tried. These were based on both common and independent dose response slopes and the confidence limits obtained from changes in deviance of a generalised linear model. The results were substantially similar and are not reported as the data are available in Table 2. Significance tests on observed complications were performed as simple 2 × 2 tables analysed by Fisher's exact test.

Results

Most of the unpremedicated children were treated on a daycase basis. They were older and weighed significantly more than the premedicated group, although there was no difference in the sex ratio between the two groups (Table 1). The dose response for loss of eyelash reflex and placement of a facemask can be seen in Table 2. ED$_{50}$ and ED$_{90}$ for loss of eyelash reflex and for tolerance of facemask for both groups of patients have been derived and shown in Table 3 and Fig. 1. It is obvious from the values of ED$_{50}$ that a larger dose of propofol is required for tolerance of facemask than for loss of eyelash reflex. The effective anaesthetic dose was also greater for the unpremedicated children for both stimuli.

The ED$_{90}$ for the loss of eyelash reflex was 2.0 mg/kg for the premedicated children and 2.8 mg/kg for the nonpremedicated group. However, for tolerance of facemask the dose required for successful induction fell well

Table 1. Patient data.

	Dosage mg/kg	Number in group	Mean age, years (SD)	Mean weight, kg (SD)	Sex F : M
Group A, premedicated	1.0	12	5.66 (3.11)	21.45 (9.94)	6 : 6
	1.5	12	5.87 (3.41)	20.62 (8.20)	4 : 8
	2.0	12	5.46 (2.57)	18.92 (5.31)	3 : 9
	2.5	12	5.72 (2.55)	21.38 (6.86)	3 : 9
	3.0	12	5.08 (1.81)	19.55 (4.28)	2 : 10
	3.5	12	5.60 (2.33)	29.51 (4.94)	4 : 8
	Total	72	5.56 (2.60*)	20.24 (6.70†)	22 : 50
Group B, unpremedicated	1.5	12	6.22 (3.23)	23.51 (11.69)	1 : 11
	2.0	12	7.31 (2.92)	24.24 (7.58)	3 : 9
	2.5	12	7.78 (3.76)	28.96 (18.44)	8 : 4
	3.0	12	7.36 (2.22)	26.68 (8.90)	6 : 6
	3.5	12	7.15 (2.95)	24.33 (10.64)	5 : 7
	4.0	12	7.16 (3.20)	26.96 (9.45)	3 : 9
	Total	72	7.16 (3.01*)	25.78 (11.41†)	26 – 46

Comparison between Groups A and B using *t*-test: * $p < 0.001$; † $p < 0.01$.

Table 2. Response to bolus doses of propofol.

	Propofol, mg/kg	Number in group	Percent with abolition of eyelash reflex	Percent who tolerated facemask
Group A, premedicated	1.0	12	42	8
	1.5	12	67	25
	2.0	12	83	33
	2.5	12	100	75
	3.0	12	100	75
	3.5	12	100	92
	Total	72	82	51
Group B, unpremedicated	1.5	12	50	33
	2.0	12	67	25
	2.5	12	83	58
	3.0	12	100	67
	3.5	12	100	50
	4.0	12	92	83
	Total	72	82	53

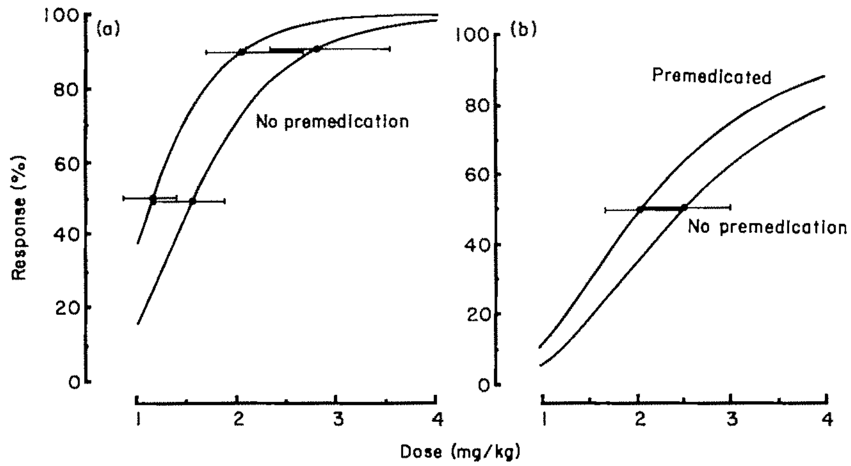

Fig. 1. Dose response curves for the premedicated and nonpremedicated groups using (a) loss of eyelash reflex and (b) acceptance of facemask as end points. 95% confidence limits.

Table 3. Dose of propofol, mg/kg, with 95% confidence limits that induced loss of eyelash reflex (ELR) and the acceptance of facemask (AFM) in 50% and 90% of the children.

		ED_{50}	ED_{90}
Group A	ELR	1.1 (0.9–1.4)	2.0 (1.7–2.7)
Group B	ELR	1.6 (1.2–1.9)	2.8 (2.3–3.5)
Group A	AFM	2.0 (1.7–2.5)	Outside range, see text
Group B	AFM	2.5 (2.1–3.0)	

Table 4. Observed complications with propofol.

	Group A (n = 71)		Group B (n = 71)		Total (n = 142)
	n	%	n	%	%
Pain on injection	21	29.2	18	25	27
Semipurposeful movements	18	25	13	18.1	21.5
Tremor/rigidity	4	5.6	7	9.7	7.6
Nausea/vomiting	2	2.8	9	12.7	7.7
Erythema	0	0	1	1.4	0.7
Headache	0	0	4	5.6	2.8

outside the chosen range of bolus doses, particularly in the unpremedicated group. Hence the values of ED_{90} for this end point could be derived only by extrapolation. This yielded an ED_{90} in group A of 4.3 mg/kg (with 95% confidence limits of 3.3–6.6 mg/kg); in group B the ED_{90} was 5.2 mg/kg (4.1–8.1 mg/kg).

The side effects of propofol are summarised in Table 4. We failed to obtain this information on two children, one from each group. Pain on injection was observed in 27% of the remainder with no significant difference in incidence between the two groups. A total of 31 children (21.5%) demonstrated semipurposeful movements during induction, while 11 (7.6%) exhibited tremor and rigidity. These excitatory phenomena were self-limiting, occurred during the first few minutes and usually disappeared as anaesthesia deepened. No patient appeared to convulse at any stage. Postoperative nausea and vomiting were more common in the unpremedicated group.

Discussion

Many different methods have been employed to assess depth of anaesthesia. Loss of eyelash reflex is used commonly as an end point when injecting intravenous induction agents. This sign indicates a fairly constant degree of cerebral depression with thiopentone.[11] However, with propofol in adults, this sign would seem to be the least reliable.[7] We therefore also used the acceptance of a facemask with, if necessary, elevation of the jaw to maintain an airway as an end point. Moreover, in clinical practice, this criterion is used commonly as an indicator of a smooth transition to maintenance of anaesthesia. Loss of eyelash reflex signifies a lighter level of anaesthesia while acceptance of a facemask represents a slightly deeper level.[12] Our data on ED_{50} (Table 3) confirm this observation where nearly 1.0 mg/kg more propofol is required to produce acceptance of a facemask in 50% of both of the premedicated and unpremedicated children.

For the loss of eyelash reflex the ED_{50} in premedicated children was 1.1 mg/kg compared with 1.6 mg/kg in the unpremedicated group. To achieve tolerance of a facemask a dose of 2.0 mg/kg or 2.5 mg/kg, respectively, was required. Eyelash reflex was lost in 90% of premedicated children with a mean dose of 2.0 mg/kg (with 95% confidence required of 1.7–2.7 mg/kg). The unpremedicated children required a mean dose of 2.8 mg/kg (with 95% confidence interval of 2.3–3.5 mg/kg). However, when acceptance of a facemask was used as an end point, statistical problems were encountered in an attempt to estimate the confidence intervals of the 90% dose. The estimated doses were outside the range of those used in this study and the confidence intervals by different methods gave dissimilar results.

It would appear from this study that a fast and reliable induction in most healthy premedicated children would be achieved by a bolus injection of propofol in a dose greater than 3.5 mg/kg. The unpremedicated children would need a dose greater than 4.0 mg/kg. Allocation to the premedication or nonpremedication group was on clinical grounds and so was not random. It is possible that differences between the two groups are caused by factors other than the presence or absence of a sedative, but it seems likely that this is the major cause of the difference observed in the study. These findings are in conformity with other studies which determined that children require larger doses of intravenous agents, whether premedicated or not,[7,13,14] compared with adult patients. In young, healthy adults a dose of propofol 2.5 mg/kg is required to achieve anaesthesia.[11,15]

Spontaneous movements are reported in 14%[16] to 33%[17] of adult patients. Similar movements were observed in 21.5% of the children in our study. There was no correlation with the dose used and the incidence of movements in either group. Semipurposeful movements occurred mostly after the end of injection and the application of a facemask, but many of these children settled without further incremental doses of propofol and after anaesthesia had been deepened with inhalational agents.

A major problem with propofol is pain on injection. The incidence of pain remains high despite the use of fat emulsion as a vehicle. In adults injection of propofol into the antecubital fossa is associated with a lower incidence of pain (2.5–6%) than when injected into the small veins of the hand (28.5–37%).[16,18] Despite the use of lignocaine which has been shown to reduce the pain of injection[16,18] we found a 27% incidence when using small veins in children. It was difficult, in the very young children used in our trial, to assess the degree of pain and also to distinguish the discomfort of injecting a cold solution into a vein from the true pain on injection. Therefore, withdrawal of the arm on injection was used as evidence of pain. Our figure of 27% is close to that of 24% found by Purcell-Jones *et al.*[8] when they used the antecubital fossa to inject propofol, without lignocaine, in children aged 3–16 years.

The reported incidence of postoperative nausea and vomiting has varied from less than 1% to 17.5%[15,19] in adults who underwent a variety of surgical procedures. We noticed an overall incidence of 7.7% of postoperative nausea or vomiting. A majority of these children were unpremedicated.

This study indicates that propofol is an effective induction agent in fit children, particularly for day cases where a short recovery time is desirable. However, a larger dose than that required for adults is needed to achieve satisfactory anaesthesia in both premedicated and unpremedicated children. Furthermore, there is a wide variation in the dose requirement. We recommend a dose of 2.5–3.5 mg/kg for induction of anaesthesia in children with titration within this range.

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CASE REPORT

Anaphylactoid reaction following the use of etomidate

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Summary

A 13-year-old female suffered urticaria and severe bronchospasm sufficient to cause hypoxic cardiac arrest after intravenous induction of anaesthesia. Etomidate was strongly implicated in the reaction. The management and mechanism of the reaction are described and discussed, together with consideration of future anaesthesia in the patient.

Key words

Anaesthetics, intravenous; etomidate.
Complications; bronchospasm, urticaria.

Each year 10 000 patients in the UK may have a clinically significant anaphylactoid reaction to anaesthetic drugs.[1] Allergic and atopic individuals often appear particularly at risk[2,3] and some drugs are more commonly involved than others.[4] The combination of etomidate, fentanyl and vecuronium has been found to be predominantly free from histamine release.[4] It is, therefore, an appropriate combination for anaesthesia in atopic asthmatic patients, but must be seen as a low risk, rather than a 'no risk' drug combination. We report a severe reaction in an asthmatic patient, following these drugs.

Case history

A 13-year-old female who weighed 33 kg, required a pleurectomy. She had had pneumonia in infancy followed throughout childhood by repeated cough and wheeze. Bronchograms at age 10 years showed cystic change in the left lung, and she had a ventilation/perfusion deficit in this area. She had had three pneumothoraces in the last year. Her usual medication was prednisolone, theophylline, long-term co-trimoxazole and salbutamol by inhalation. She had had one uneventful exposure to thiopentone, suxamethonium, nitrous oxide and halothane and had no known allergies.

She arrived in the operating theatre crying after premedication with lorazepam 1 mg and inhaled salbutamol. A needle was sited in her hand and etomidate 10 mg, fentanyl 0.2 mg and vecuronium 4 mg were given. Ventilation was attempted with the aid of several types of airway and mask, a tracheal tube and a bronchoscope with Sanders injector, but proved impossible. The view down the bronchoscope showed both main bronchi clamped shut. The chest was exposed and wheals were seen. An intravenous infusion of crystalloid was established and hydrocortisone 100 mg and chlorpheniramine 10 mg were given intravenously. Ventilation of the lungs remained impossible and bradycardia was followed by cardiac arrest. The pulse returned after adrenaline, 0.2 mg given intravenously, and ventilation was possible. A size 6.0 mm tracheal tube was passed and she became pink with an arterial blood pressure of 120/80 mmHg.

The patient was now paralysed, but had received no volatile agents since induction. Etomidate 10 mg was therefore given to maintain sleep and within 2 minutes her lungs were impossible to ventilate, with cyanosis and bradycardia ensuing. Adrenaline 0.1 mg administered intravenously brought rapid relief; enflurane was added to the oxygen to achieve anaesthesia. The operation was abandoned. Muscle relaxation had worn off and after much deliberation, vecuronium 2 mg was given with no ill effect. Admission to the Intensive Care Unit was arranged and initially the urticaria worsened with pronounced oedema around the eyes. By one hour this was clearing and by 2 hours arterial blood gases were normal. She made an uneventful recovery and has since remained well. The pleurectomy has not been rescheduled.

Sequential blood samples were collected in EDTA tubes

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over 24 hours, for analysis by the National Adverse Anaesthetic Reaction Advisory Service, Sheffield. These showed highly raised plasma IgE levels of > 1000 units/ml, consistent with an atopic patient, but no indication of the mechanism of response. The Committee on Safety of Medicines was notified by 'yellow card'.

Discussion

This paper reports a near fatal case of bronchospasm after drugs thought to be free from histamine release.[5–7] We chose etomidate, fentanyl and vecuronium because of the patient's asthma and the increased risk of reaction. There has been one previous death following this combination, also in a young severely asthmatic patient,[4] but no one drug was implicated.

The observed bronchospasm, urticaria and facial oedema soon after drug administration, lasting for one hour, and responding to adrenaline, is typical of a drug-induced anaphylactoid reaction. Etomidate appears to be implicated clinically in this case. The two reactions had the same manifestations and the same time relationship to drug administration. No significant histamine release has been noted with etomidate alone,[5] although repeat administrations with muscle relaxant have shown clinical signs consistent with histamine release.[8] The few genuine reports of reaction to etomidate may involve synergy with muscle relaxants. Cutaneous manifestations, cardiovascular stability and noninvolvement of complement pathways[9] have been noted and are in keeping with this case, but severe bronchospasm has not been reported.

Vecuronium appears to be safe in this patient on the basis of the uneventful second administration, and it is reputed to be free from histamine release,[6] but severe bronchospasm has been reported following its use.[10] Possible mechanisms for this reaction should be considered. The blood investigations confirmed an atopic tendency, with very high IgE levels, but she lacked previous exposure to the precipitating drug. Direct release of histamine, or other immune mediators (kinins, prostaglandins, serotonin or slow reacting substance of anaphylaxis A) by the drug, remains the most likely possibility. This kind of reaction is exacerbated frequently by the speed of injection and dose of drug.[11] The dose of etomidate 0.3 mg/kg was in accordance with the data sheet, but it was injected quickly, so drug levels within the lung would be high.

A pleurectomy may still be necessary for this patient, and there are many other conditions for which she might require general anaesthesia. A regional technique would be attractive if surgery allowed. Etomidate must be avoided, whatever the mechanism of response, and an inhalational induction would be safer than the use of other intravenous hypnotics. There is no safer alternative to fentanyl if analgesia is required. Vecuronium would seem to be suitable, with pancuronium or atracurium as alternatives. Atracurium produces cutaneous flushing although histamine release seems to be confined to the skin.[12]

Anaphylactoid reactions will still happen, in spite of the best preparations and considerations, and one must always be ready to recognise and treat them. Recently Fisher *et al.*[13] have advanced the point of view that although there is a greater incidence of asthma, atopy and allergy among those suffering anaphylaxis, the incidence is so low that history alone is not a reliable predictor of reaction in an individual. Serious reactions to etomidate are rare, and it may be that with time, more cases will emerge, giving both a clue to the mechanism of response or the patient at particular risk.

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CASE REPORT

Anaphylactic reaction after atropine

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Summary

A 38-year-old woman developed symptoms of anaphylactic shock after intravenous atropine and required adrenaline to maintain perfusion pressure. A strongly positive response was obtained on intradermal testing. The Prausnitz–Kuestner test was also positive, which indicated the presence of drug specific IgE antibodies. No response was obtained after hyoscine.

Key words

Allergy.
Parasympathetic nervous system; atropine.

Adverse drug reactions during anaesthesia appear to be on the increase,[1] and include those of allergic origin.[2] The true incidence is unknown; Watkins estimates that 5000–10 000 occur in the UK each year, while Fisher and More[3] report an incidence of 1/5000 to 1/20 000 cases, with an associated mortality of 3–4 %. The increase in the incidence of allergic reactions in the last few years is undisputed.[4] This is attributed to the greater number of drugs used peri-operatively, multiplicity of exposure to the same or related drugs and a history of chronic atopy.[5]

The terminology that relates to allergic reactions has also been clarified.[6] For an anaphylactic reaction to occur, previous exposure to the drug (or similar agent) is necessary. This results in the production of specific antibodies or the interaction of specifically sensitised T-lymphocytes with the specific antigens. Re-exposure then induces release of chemical mediators from basophils and mast cells, and thus produces the reaction. The nonimmune anaphylactoid reaction results from the interaction between the agents and cells which triggers a release of histamine; previous exposure is not necessary. Occasionally both types of reaction are implicated,[5] and it is only possible to separate them by specific laboratory tests.[7]

We report here a reaction after intravenous administration of atropine, where later laboratory evaluation indicated the occurrence of an anaphylactic reaction.

Case history

A 38-year-old, 72-kg woman with no history of allergy or atopy was scheduled for varicose vein surgery under spinal anaesthesia. Flunitrazepam 2 mg was given the evening before surgery. Her arterial blood pressure was 100/60 mmHg and heart rate 68 beats/minute in the anaesthetic room. An infusion of Hartmann's solution was started and she was given atropine 0.01 mg/kg intravenously. She became anxious shortly afterwards and developed generalised urticaria and pruritus. Her arterial pressure was 90/60 mmHg and heart rate 110 beats/minute. She then developed intense abdominal pain with nausea and vomiting. Peripheral pulses became impalpable and the heart rate increased to 170 beats/minute.

She was placed in a head-down position and given oxygen. The infusion of Hartmann's solution was increased. Hydrocortisone 1 g and calcium chloride 1 g were given intravenously followed by 0.5 mg adrenaline subcutaneously. Twenty minutes later the arterial pressure had increased to 110/80 mmHg and the heart rate had decreased to 120 beats/minute. Generalised urticaria with facial and eyelid oedema were present, together with severe pruritus. Antihistamines and steroids were continued and after 2 days the cutaneous signs had disappeared. The only abnormal laboratory findings were then a blood glucose of 1.92 g/litre and a leucocytosis of 23 000.

Blood for IgE levels was taken 1, 6, 24 and 48 hours after the injection of atropine and the results were 28, 32, 35 and 39 units/ml respectively (normal values up to 110 units/ml). One month after this event an intradermal test to atropine 1:100 was strongly positive. Tests to antigens Hbs, HTLV III and VDRL were negative. Two months after the event, the Prausnitz–Kuestner test was performed; her husband was the receptor. A sample of the patient's

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plasma was placed in two tubes, one of which was frozen to −70°C and the other incubated at 56°C for 4 hours to destroy IgE. The next day 0.1 ml of both samples was administered intradermally to the receptor. Forty-eight hours later 0.05 ml of atropine (strength 1:100), from the same batch that provoked the reaction, was administered into the same intradermal sites. A positive reaction was obtained at the site of the plasma stored at −70°C, but not at the other. The husband's IgE levels were not measured. On questioning, the patient admitted occasionally taking a pharmacological compound that contained atropine up to one year before the episode. An intradermal test to hyoscine was negative.

Discussion

Many authors have reported adverse reactions after atropine,[8–13] and development of an erythematous rash over the face, neck and upper chest is common. This may be an allergic reaction, but is of no clinical significance. Clinically, allergic reactions involve many organs. The severity of the symptoms (Table 1), the onset and duration are extremely variable. An allergic reaction occurs rapidly and tends to be severe[6] after intravenous drug administration, as in our patient. Oral ingestion of the antigen may subsequently produce symptoms.[14] Histamine is the essential chemical mediator after anaphylaxis, although at least 20 other chemicals are involved.[5]

Table 1. Grades of severity of allergic reactions.

Grade	Clinical features
1	Cutaneous feature, erythema, urticaria, flushing, abdominal pain
2	Tachycardia, hypotension, bronchospasm
3	Cardiovascular collapse
4	Cardiac arrest

The initial symptoms are cutaneous[11] as a result of histamine-provoked capillary dilatation and increased permeability, and usually occur over the face and neck. These lesions disappear in a few days.[4,9] The abdominal manifestations are caused by increased peristalsis,[6,15] but are often masked in anaesthetic practice since the patients are usually anaesthetised. The severe hypotension is caused by acute vasodilatation and reduction in circulating volume, as a result of increased capillary permeability. The tachycardia arises from release of catecholamines, which may also be the cause of resultant dysrhythmias.[16] The reported incidence of cardiovascular collapse after allergic reactions varies. Le Cam *et al.*[9] report an incidence of only one in 5000. This is in contrast to Fisher and Baldo,[11] who reported that cardiovascular collapse was the commonest life-threatening feature in 82% of patients. Unusually, bronchospasm did not occur in our patient.

A severe allergic reaction requires prompt and aggressive treatment.[2,5,6] The volume deficit was corrected and steroids and calcium were given to our patient but adrenaline was still required to restore the circulation. Improvement has been reported after isoprenaline and diphenhydramine,[5,6] while metaraminol has been suggested[11] since it is less likely to precipitate dysrhythmias in the presence of volatile anaesthetic agents.

It is incumbent upon the anaesthetist to try to determine the drug responsible after an allergic reaction. The various methods available are listed in Table 2, although intradermal testing is probably the easiest and most reliable method.[11,17] A reaction began immediately after atropine administration in our patient. Atropine has been reported to produce an anaphylactoid reaction[9] and an entirely cell mediated response.[18] Intradermal testing was strongly positive, and resulted from histamine release.[19] The Prausnitz–Kuestner test revealed a positive response to the non-heat treated sample, which suggested the presence of IgE antibodies for atropine and confirmed the occurrence of an anaphylactic reaction.

Table 2. Diagnostic tests after allergic reactions.

Primary diagnosis, clinical features	Secondary diagnosis, risk factors
Routine laboratory tests	*In vivo tests*
Plasma IgE levels	Intradermal tests
Plasma histamine levels	Passive transfer (e.g. Prausnitz–Kuestner)
Complement levels	
Basophil count	
	In vitro tests
	Leucocyte migration inhibition test
	Lymphoblast transformation test
	Radiollergosorbent test
	Leucocyte histamine liberation test
	IgE inhibition test

The patient admitted taking an oral proprietary analgesic compound which contained 0.25 mg atropine up to one year before the event. This exposure could have produced the IgE antibodies; the atropine acted as a hapten since it itself has a low molecular weight (624.8). It is possible for a patient to be exposed repeatedly to a drug and eventually develop an allergic reaction.[6] A reaction was provoked in our patient because the intravenous administration of atropine resulted in much higher plasma levels than would be reached after oral intake. Hyoscine has been proposed as an alternative to atropine in these patients,[20] and was shown to be safe in this case by intradermal testing. Glycopyrronium could also be used after testing.[21,22]

We conclude from the results of the tests performed that this patient had an anaphylactic reaction to atropine mediated by IgE antibodies.

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Anaesthesia, 1988, Volume 43, pages 958–961

CASE REPORT

Fatal anaphylactic reaction to suxamethonium: new screening test suggests possible prevention

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Summary

A 40-year-old woman suffered cardiovascular collapse, cardiac ischaemia and arrest during induction of anaesthesia. Severe cerebral ischaemic damage was sustained during this episode and the patient died 4 days later. This fatal reaction was shown to be anaphylactic in origin; the causative agent was suxamethonium. High levels of IgE antibodies specific to the quaternary ammonium group (two of which are present in suxamethonium) were detected by the radioallergosorbent test. Results of the leucocyte histamine release test were less clear, partly as a result of steroid treatment. The two most relevant points were the absence of a history of previous anaesthesia, and involvement of the heart as the principal target of the reaction. This unfortunate and extreme case indicates the necessity for allergy testing (screening) before anaesthesia, and the need for organisation and funding of this procedure, if these fatal or near-fatal reactions are to be prevented. It is a timely reminder that action should be taken, since neuromuscular blockers have been confirmed as the most common culprits, and that specific tests for IgE antibodies are now available against haptenic groups generally common to all neuromuscular blockers.

Key words

Neuromuscular relaxants; suxamethonium.
Allergy; anaphylaxis.

Severe anaphylactic reactions to anaesthetic agents are rare, but seem to contribute significantly to anaesthetic mortality and morbidity.[1,2] In theory, these reactions are at least partly preventable, if a diagnostic or screening procedure can be applied to a selected section of patients who appear to be particularly at risk. A potentially useful screening procedure is now available, but patient selection is a difficult task because a major proportion of those who react give no history of prior exposure.[2–8] A reaction that occurs when a drug is given for the first time suggests a nonimmune mechanism; hence the use of the terms 'anaphylactic-like' or 'anaphylactoid'. However, it has now emerged that IgE antibodies may be detected in the latter type of reaction,[4–8] and this suggests prior and largely unknown exposure to closely related (cross-reacting) immunogens (haptenic determinants in the case of drugs which are simple chemicals). At present, neuromuscular blockers (NMB), seem to be the most common culprits: a bis-quaternary ammonium (at least two quaternary ammonium groups) structure is an essential component of the molecule of NMBs which cause such a reaction.[9]

Case history

The patient, a 40-year-old woman, was admitted to hospital for routine total abdominal hysterectomy. She had no past history of operations (except for an uneventful dental chair intravenous anaesthetic) or allergies. Her medication comprised danazol for the treatment of uterine bleeding and bendrofluazide for mild hypertension. She had occasional dyspepsia and frequent headaches, for which she took non-narcotic analgesics and had undergone a course of treatment with meprobamate. She was a nonsmoker. One of her two children (son 20 years) suffers from penicillin allergy, and her two sisters suffer from minor contact allergies, but all had received uneventful general anaesthetics.

Pre-operative examination revealed a mild iron deficiency anaemia with a haemoglobin concentration of 10.3 g/dlitre, normal white cell and platelet counts, and a normal chest X ray, Vitalograph and electrocardiograph (ECG). The patient was slightly overweight at 70 kg (height 155 cm). She was considered to be fit for surgery.

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Premedication consisted of intramuscular papaveretum 10 mg, hyoscine 0.2 mg and metoclopramide 10 mg. Anaesthesia was induced with thiopentone 350 mg, followed immediately by suxamethonium 60 mg. Lignocaine throat spray was used and the trachea was intubated easily. The lungs were inflated with oxygen 100%, followed by N_2O/O_2 (4 litres/minute of each) and 1% halothane through a Bain system. The skin became flushed with bright red colour and showed a 'goose-pimple' appearance within 90 seconds of her induction. A tachycardia with a heaving cardiac impulse was noted, and there was difficulty in inflation of the lungs. Jerky, tugging respiration started within another 20 seconds. The position of the tracheal tube was checked, anaesthetic gases were discontinued and oxygen 100% was given. An ECG and Datascope monitor were attached and showed a sinus tachycardia of 100–110 beats/minute and systolic arterial pressure of 110 mmHg. An infusion of sodium chloride 0.9% was started and hydrocortisone 50 mg was given intravenously. The patient appeared to improve momentarily, but suddenly (about 10 minutes after induction) the red colour changed to slate-blue, the arterial pressure decreased rapidly, and the peripheral pulse became impalpable. The patient stopped breathing and the ECG showed severe bradycardia, as the heart rate decreased rapidly from 100 to 10 beats/minute. Cardiopulmonary resuscitation (with external cardiac compression) was started and two consecutive doses of atropine, 0.6 mg each, were given into a fast intravenous infusion, followed by 10 ml of 1/10 000 adrenaline. Another intravenous infusion was started and 8.4% sodium bicarbonate was given (total infusion 120 mmol), followed by rapid infusion of 500 ml polygeline (Haemaccel). Cardiac action was restored and developed rapidly to a sinus tachycardia of 120–152 beats/minute; systolic arterial pressure increased to 70–80 mmHg. A 100 mg bolus injection of hydrocortisone was given intravenously, followed by an infusion of dopamine and polygeline. Spontaneous breathing resumed and the arterial pressure was restored gradually to normal. The patient opened her eyes on two occasions, but became comatose, the pupils dilated and fixed. A 12-lead ECG one hour after the episode showed widespread ischaemic changes. The conjunctivae became oedematous, and frusemide 10 mg was given intravenously. She was transferred to the Intensive Care Unit of the Whittington Hospital when her condition was as stable as possible, where she remained in coma and was maintained on intermittent positive pressure ventilation until she was finally declared brain-dead 4 days later.

Further investigations

A leucocyte histamine release test was carried out twice (on the third and fourth days after the reaction) according to the method described previously by Assem *et al.*[10] The patient at that time was still receiving hydrocortisone 100 mg intravenously 6-hourly. Estimation of total serum IgE, complement C3 and C4, complement conversion fragments C3b and C3d, C1-binding immune complexes, and complement C1 esterase-inhibitor were all determined on blood samples collected on the third or fourth days, and some of these were also measured in a serum sample that had been collected 2 days before the reaction. Stored serum samples were tested a few months after the patient's death for specific IgE antibodies against the quaternary ammonium haptenic group, by the radioallergosorbent test (RAST, a collaborative project with Pharmacia Ltd). In addition, cardiac tissues were collected at autopsy and examined for the presence of mast cells and their sensitisation with IgE.

Results

Figure 1 shows the results of the leucocyte histamine release tests. In the first, there was significant release (unexpectedly) with hyoscine, a small and insignificant release with suxamethonium, but no release with thiopentone. The scatter of results did not allow any further analysis. Consequently a second test was carried out on the same blood sample, which was by then 24 hours old. Modifications

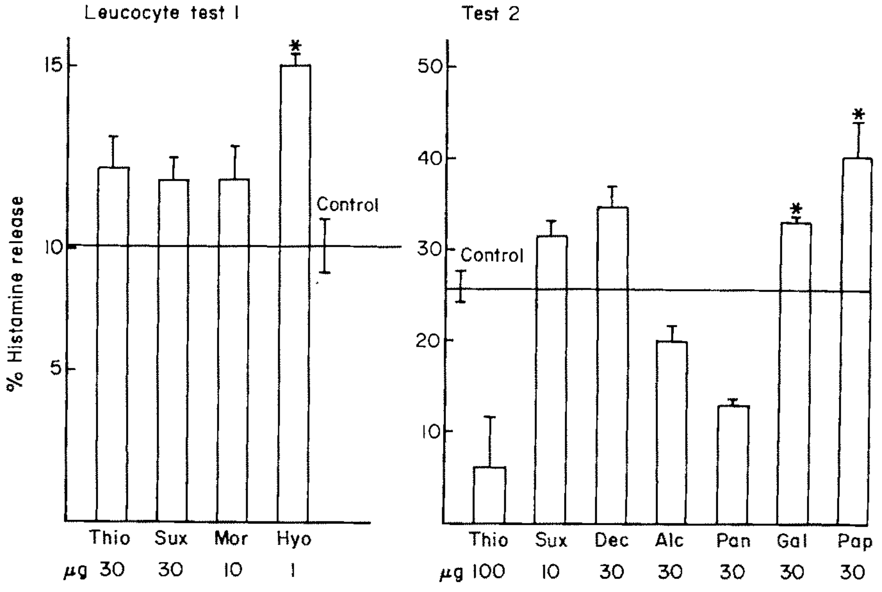

Fig. 1. Results of the two leucocyte histamine release tests which were carried out. Bars represent SEM. Thio, thiopentone; sux, suxamethonium; mor, morphine; hyo, hyoscine; dec, decamethonium; alc, alcuronium; pan, pancuronium; gal, gallamine; pap, papaveretum. * $p < 0.05$ above control.

were introduced: the use of papaveretum rather than morphine, more than one NMB, and a repeat of thiopentone. This second test showed significant release with papaveretum and gallamine, but the release by suxamethonium remained insignificant. The results seemed to confirm the occurrence of an anaphylactic or anaphylactoid reaction, with two possibilities: an unusual multiplicity of causes (papaveretum, hyoscine and, possibly the NMB suxamethonium, as suggested indirectly by the significant release with gallamine); or by treatment with hydrocortisone inhibition of the *in vitro* reaction (a documented phenomenon)[11] which would explain the low histamine release.

RAST for detection of hapten-specific IgE. The RAST for quaternary ammonium-specific IgE eventually confirmed that the patient had experienced a truly anaphylactic reaction to suxamethonium. This test was carried out on the patient's serum 6 months after her death, and was found to be strongly positive. There was a high uptake of ^{125}I-labelled anti-human IgE by a conjugate of choline (a quaternary ammonium compound) to paper discs ('allergen' discs) that had been pre-incubated in the patient's serum; 12.3% of the total amount of radioisotope labelled anti-IgE was taken up, compared to an uptake of 0.1–0.3% by allergen discs that were pre-incubated in human umbilical cord serum (which contains no IgE), or other control sera. The results of other immunological investigations were either negative or inconclusive.

The findings at postmortem were consistent with brain death, with extensive necrosis of both cerebral hemispheres, cerebellum and brain stem. There was widespread arterial and venous thrombosis, including the right internal carotid. Apart from subendocardial haemorrhages in the left ventricle, the heart and coronary vessels were normal. Autopsy specimens of cardiac tissues fixed in Carnoy's fluid, but not in formol-saline, and stained with alcian blue (and counterstained with safranin) showed the presence of mast cells in the interstitium and perivascular connective tissue. The cytoplasmic granules of these cells were alcian blue-positive/safranin-negative. These findings demonstrate not only the presence of mast cells in cardiac tissue, but also suggest that human cardiac mast cells contain a sulphated glycosaminoglycan (which is stored together with histamine in the granules) other than heparin.[12] In order to demonstrate the sensitisation of cardiac mast cells with IgE, the immunoperoxidase technique[13,14] was applied. Sensitisation with IgE was confirmed (details to be published elsewhere).[14]

Discussion

The results demonstrate the value of RAST, which is simple to perform when the material is available. The leucocyte histamine release test was of little value in this patient but it still has a place in studying individual cases, and testing for crossreactions. Complement studies, even when carried out on repeated plasma collections (e.g. 1, 6, 24 and 72 hours after the reaction, with EDTA added to stabilise complement) are unlikely to be of great value, particularly in IgE mediated reactions. This unfortunate case also demonstrates some even more important points. It has confirmed that sensitisation may occur 'spontaneously' in predisposed patients who develop IgE antibodies to cross-reacting substances; these are difficult to identify, but in the case of NMB they presumably possess quaternary ammonium groups. The future will reveal whether screening for these antibodies is feasible as a preventive measure. In addition, this case has shown that the heart is a principal and possibly a primary target of the anaphylactic reaction. Mast cells sensitised with IgE antibody would react to the specific allergen by releasing various mediators which are capable of causing cardiac dysfunction. The three most important mediators are histamine; the arachidonic acid metabolites leukotrienes (C_4, D_4 and E_4; slow-reacting substance of anaphylaxis), thromboxanes (A_2 is particularly important) and prostaglandins; and another lipid mediator called platelet-activating factor (PAF). Histamine is arrhythmogenic, and may block atrioventricular conduction, while the lipid mediators may cause coronary vasoconstriction and either a direct or indirect negative inotropic effect.[15,16]

Addendum

Since the submission of the manuscript, sera from the deceased patient's son, daughter and two sisters have been screened by RAST (at their own request); all results were negative.

Acknowledgments

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Anaesthesia, 1988, Volume 43, pages 962–963

CASE REPORT

The prolonged use of atracurium in a patient with tetanus

S. J. PEAT, D. R. POTTER AND J. M. HUNTER

Summary

A case of a patient with tetanus is reported in whom an atracurium infusion and artificial ventilation were needed in addition to sedation to control the muscle spasms. The atracurium infusion was used for 71 days, the longest time ever recorded, at a mean rate of 1.3 mg/kg/hour at the end of infusion. The plasma atracurium and laudanosine concentrations were 1.5 μg/ml and 0.985 μg/ml respectively. Subsequently there was an exponential decline in the serum laudanosine concentration which had decreased to 0.014 μg/ml 24 hours later. These results suggest that prolonged use of atracurium by infusion is not associated with excessive cumulation of laudanosine when renal and hepatic function are normal.

Key words

Neuromuscular relaxants; atracurium.
Infection; tetanus.

Case history

A 35-year-old intravenous drug abuser was admitted with muscle pain, back stiffness and inability to open his mouth. The diagnosis of tetanus was suspected and treatment with benzylpenicillin, metronidazole and antitetanus immunoglobulin was started. Severe spasms began 16 hours after admission, and could not be controlled by diazepam and baclofen. The patient was therefore anaesthetised with etomidate, paralysed with atracurium, his trachea intubated and his lungs ventilated. His venepuncture sites were debrided and irrigated with hydrogen peroxide under general anaesthesia.

Infusions of midazolam and pethidine were started after surgery, but adequate ventilation proved impossible because of the severity of the muscle spasms. An infusion of atracurium was started which controlled the spasms and allowed satisfactory ventilation. The atracurium infusion was stopped for one hour every 7 days in order to allow full patient assessment, and the dose of pethidine was reduced gradually. Atracurium was required for a total of 71 days at a mean rate of 1.3 mg/kg/hour. Strong tetanic spasms returned within 30 minutes of stopping the infusion during the first 9 weeks of treatment. There was never any clinical evidence of seizures, but electroencephalography (EEG) was not undertaken. There were periods of marked autonomic instability, manifested by tachycardia, hypertension, sweating and salivation, despite heavy sedation. However, he showed a gradual progressive improvement; autonomic function returned to normal 10 weeks after admission and only mild spasms elicited by tactile stimulation occurred when the atracurium infusion was finally stopped. He was weaned easily from mechanical ventilatory support on to a continuous positive airway pressure system, but required ventilatory support at night for 2 days after the atracurium infusion was finally stopped.

Biochemical values on admission were as follows: urea 7.9 mmol/litre (normal range 3.3–6.7 mmol/litre); creatinine 105 μmol/litre (normal range 45–105 μmol/litre); albumin 42 g/litre (normal range 35–50 g/litre); bilirubin 15 μmol/litre (normal range 3–20 μmol/litre); alkaline phosphatase 117 IU/litre (normal range 30–85 IU/litre); aspartate transaminase 70 IU/litre (normal range 10–50 IU/litre), gamma glucuronyl transferase 75 IU/litre (normal range 5–55 IU/litre). Renal and hepatic function remained normal or showed only mild impairment throughout the duration of treatment.

A 2-ml blood sample was taken for measurement of plasma atracurium and laudanosine concentrations 71 days after the atracurium infusion was started. The atracurium infusion was then stopped and blood taken for the measurement of atracurium and laudanosine concentrations approximately 2, 4, 6, 8, 10, 19 and 24 hours later. The heparinised samples were centrifuged immediately after collection and the plasma (0.2 ml) was added to 0.8 ml of 0.15 molar sulphuric acid and stored at −20°C until

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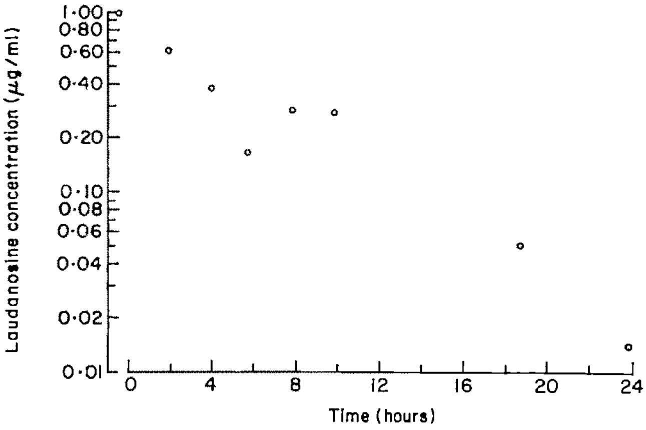

Fig. 1. A semilogarithmic plot of the plasma laudanosine concentrations for 24 hours after the atracurium infusion was stopped (at time zero).

assayed. All samples were acidified within 1.5 minutes. The method used for the assay of atracurium and laudanosine concentrations was that reported by Simmonds.[1]

The plasma atracurium concentration at the end of the infusion was 1.5 µg/ml and the laudanosine level 0.985 µg/ml. The plasma laudanosine concentration had decreased to 0.014 µg/ml at 24 hours. The semilogarithmic plot of laudanosine concentration against time (Fig. 1) demonstrates that the elimination half-life for laudanosine at the end of the infusion was approximately 180 minutes.

Discussion

The use of atracurium by infusion to facilitate ventilation of the lungs during intensive therapy has been found to offer significant advantages over other neuromuscular blocking drugs. The cardiovascular stability and lack of cumulation of atracurium make it an attractive choice for long-term use, particularly if rapid assessment of the patient is desired.[2,3,4] However, there has been concern over the possible cumulation of the metabolic products of atracurium, particularly laudanosine. This compound is a glycine antagonist with strychnine-like effects and has a mean (SD) elimination half-life in normal man of 197 (38) minutes.[3,5] Studies in conscious dogs have shown that bolus doses of laudanosine (2 mg/kg) or laudanosine infusions sufficient to produce a plasma concentration of around 1.2 µg/ml are not associated with fits. However, plasma concentrations of more than 6 µg/ml caused increases in EEG frequency and amplitude in anaesthetised dogs subjected to a laudanosine infusion, and epileptiform changes occurred at plasma concentrations that exceeded 14 µg/ml.[6]

Peak plasma laudanosine concentrations after bolus doses of atracurium (0.3–0.4 mg/kg) in man are in the range 0.2–0.3 µg/ml, and predictions based on data taken from bolus kinetic studies suggest that laudanosine concentrations could reach 1.0 µg/ml after a 20-hour atracurium infusion at 0.6 mg/kg/hour in patients with normal renal and hepatic function.[5] Much higher infusion rates (up to 1.22 mg/kg/hour) have been needed in the intensive therapy unit to provide a modest degree of block, particularly in oedematous patients, and it has been suggested that a further increase in atracurium requirement may occur after the first 72 hours of infusion.[3,4] Such high doses of atracurium given by infusion might be expected to cause an increase in the steady state laudanosine plasma concentration, particularly in patients with significant hepatic and renal impairment.[5] Consequently, there has been concern about the possibility of cerebral irritation during long-term use of atracurium. However, the cerebrospinal fluid: plasma ratio is lower in man than in the dog[7] and no clinical reports of such irritation have yet been reported.

This case report demonstrates that plasma laudanosine levels did not reach those associated with EEG changes in anaesthetised dogs, even after prolonged use of a large dose of atracurium given by infusion to a patient with normal renal and hepatic function, and that laudanosine was cleared from the plasma at a rate comparable with that reported after bolus doses of atracurium.[5]

Acknowledgments

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Anaesthesia, 1988, Volume 43, pages 964–966

CASE REPORT

Multiple rib fractures and head injury—an indication for intercostal catheterisation and infusion of local anaesthetics

P. J. GRAZIOTTI AND G. B. SMITH

Summary

A case is presented which demonstrates the advantages of continuous intercostal analgesia in a patient with a head injury and multiple rib fractures.

Key words

Anaesthetic techniques, regional; intercostal.
Analgesia; rib fractures.

Intercostal catheterisation and infusion of local anaesthetics (extra- or intrapleural analgesia) is a relatively new technique for the management of patients with multiple rib fractures.[1,2] Intravenous opioids or thoracic epidural analgesia would be equally satisfactory in the majority of such cases.[3] This is not so in patients with coexisting head injury and raised intracranial pressure; intravenous opioids make neurological assessment difficult and a dural tap could be potentially fatal.

A case is presented in which intercostal catheterisation and infusion of local anaesthetics was used in these circumstances to provide very effective analgesia.

Case history

A 46-year-old previously fit man fell from a ladder (from a height of 6 metres) and sustained head and chest injuries. He had a grand mal fit during transfer to hospital. His conscious state was depressed on admission [Glasgow Coma Scale (GCS) 8] but improved (GCS 11) over 3 hours. Skull and cervical spine X rays showed no fractures. A chest X ray showed fractures of the third to tenth ribs on the left with some pleural fluid over the apex of the left lung. The serum potassium concentration was 2.6 mmol/litre; other electrolyte concentrations were normal. Arterial blood gas analysis revealed: pH 7.34; $P\text{aco}_2$ 5.1 kPa; $P\text{ao}_2$ 8.6 kPa ($F\text{io}_2$ 0.6). The electrocardiogram was normal. His conscious state was normal 12 hours after admission, but hypoxaemia persisted; consequently his trachea was intubated and his lungs were ventilated. His $P\text{ao}_2$ improved to 11 kPa ($F\text{io}_2$ 0.4). High doses of opioids were necessary to allow physiotherapy and this made assessment of his conscious state difficult. There was no evidence of cerebral oedema.

A thoracic epidural was inserted at the T_{6-7} interspace and a continuous infusion of bupivacaine 0.25% 3 ml/hour with fentanyl 6 μg/hour (100 μg per 50 ml of bupivacaine) provided excellent analgesia. Intravenous analgesia was stopped and physiotherapy was tolerated without problems.

The trachea was extubated 2 days later. His conscious state deteriorated markedly a few hours after extubation and he developed neck stiffness, a positive Kernig's sign and a temperature of 40 °C. The $P\text{ao}_2$ decreased to 8.8 kPa.

The epidural catheter was removed because of the possibility of infection; culture of the tip was negative. His trachea was reintubated and he was transferred to the regional neurological centre for computerised tomography which showed diffuse cerebral oedema; he was then sent back to our hospital. Analgesia was still necessary, but we were advised by the regional neurosurgical centre that the risks of dural puncture contraindicated epidural injection. Intracranial pressure measurement was not available. The use of intravenous opioids was considered to be inappropriate as this may make neurological assessment difficult.[4] An intercostal catheter was therefore inserted with the patient lying on his right side. An 18-gauge brachial plexus needle and catheter were used. The needle was 'walked' off the lower edge of the angle of the sixth rib and advanced 2–3 mm through the posterior intercostal membrane. Seven centimetres of the catheter were inserted. An anteroposterior chest X ray was taken after the introduction of 5 ml of contrast medium, and showed that the cath-

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eter extended cephalad over three ribs and that dye spread cephalad and caudad over three ribs. Twenty millilitres of plain bupivacaine 0.25% were injected through the catheter and an infusion of 3 ml/hour of the same solution was started. Intravenous analgesics were stopped. Sensory testing later showed a slight loss of pinprick between T_2 and T_4. Analgesia was excellent and full physiotherapy was possible. Serum bupivacaine concentrations were 0.4 μg/ml after 24 hours. Extubation was undertaken 2 days later and the intercostal catheter was removed one week after its insertion. He made a full and uneventful recovery.

Discussion

Intercostal catheterisation for multiple rib fractures was first described by O'Kelly and Garry.[1] The authors of subsequent studies have attempted to identify the best technique to locate the extrapleural[5,6] or intrapleural[2,7] space, the optimum length of catheter to leave *in situ*,[5] the ultimate position of the catheter,[5,8,9] the ideal solution to inject[2,10] and the site of action of that solution.[2,5,6,8–13].

Catheters are inserted usually through a Tuohy needle at the angle of the rib or a fixed distance (8–10 cm) from the midline posteriorly. Identification of the extrapleural space is achieved usually by advancement of the needle 3–4 mm beyond the lower rib edge, through the posterior intercostal membrane. In practice, this membrane can be difficult to feel and most catheters possibly lie intrapleurally.[6] Rocco *et al.*[2] describe a technique to identify the intrapleural space by using a well lubricated syringe attached to a Tuohy needle. They 'walk' the needle off the upper edge of the rib and entry into the pleural space is indicated when the plunger of the syringe is drawn inward by the negative intrapleural pressure. No attempt was made in that study to determine the ultimate position of the catheters. However, all nine patients, each of whom had multiple rib fractures, obtained complete pain relief. There was one pneumothorax.

Some studies have attempted to identify the position of catheters.[5,8,9] Murphy[8] used O'Kelly and Garry's method[1] in cadavers. He directed 3–4 cm of catheter medially after the needle had passed through the posterior intercostal membrane; 18 of the 24 catheters were placed extrapleurally, and one was too superficial. A radiographic study in which the same technique was used but in which the catheters were directed laterally resulted in extrapleural placement of the catheters in nine of 12 attempts.[9] The radiographic criteria used to determine correct placement have since been questioned.[6] Mowbray *et al.*[5] directed the catheters medially in patients who were about to undergo thoracotomy or median sternotomy. At operation, only 12 of the 22 catheters were definitely placed correctly; easy advancement of the catheters beyond 3 cm was associated with intrapleural catheterisation. Thus it would seem that the catheter in our patient was probably intrapleural.

Bupivacaine was used in all the studies of intercostal catheters for analgesia. A 20-ml bolus of bupivacaine 0.5% is followed usually by an infusion of bupivacaine 0.5% or 0.25% at a rate of 10 ml/hour. Intercostal bupivacaine is absorbed rapidly,[11] and peak concentrations are often more than 2.0 μg/ml;[2,7,15] concentrations of up to 3.26 μg/ml were found in one study.[7] The blood concentration of bupivacaine at which toxicity occurs varies, but bupivacaine concentrations in excess of 1.6 μg/ml are usually associated with mild toxic symptoms.[16] Hypoxaemia and acidosis enhance bupivacaine toxicity and these conditions are likely to be present in patients with multiple fractured ribs. However, Rocco *et al.*[2] found that an infusion of bupivacaine 0.25% at a rate of 5 ml/hour was inadequate to control pain in one of his patients. Bupivacaine with adrenaline may have a longer duration of effect[2] and result in lower (but still high) blood concentrations.[15] We used bupivacaine 0.25% at a rate of 3 ml/hour; blood concentrations were well below toxic levels, and satisfactory analgesia was achieved.

The site of action of solution injected through an intercostal catheter has been the subject of many studies.[2,5,6,8–13] Cadaveric dye studies have examined extrapleural spread only and concluded that the dye is either contained in the intercostal space[12] or spreads extrapleurally and/or into the paravertebral space.[8,11] Other studies, in which a variety of techniques was used, have confirmed extrapleural and paravertebral spread.[5,9,13] The site of action of intrapleural solutions has been the subject of conjecture only; Bruce *et al.*[10] consider that the site of action is the intercostal nerve which is reached by retrograde diffusion through the parietal pleura.

Intercostal catheterisation with infusion of local anaesthetics intra- or extrapleurally is currently popular in the management of postoperative pain and pain caused by multiple rib fractures. There is no contraindication to other well established forms of analgesia in many patients. However, intercostal catheterisation may have advantages in the management of patients with injuries to the head and chest. Further research is necessary to establish safe and effective infusion rates.

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Anaesthesia, 1988, Volume 43, pages 967–969

CASE REPORT

Pulmonary oedema following carbamazepine overdose

G. E. KITSON AND T. D. WAUCHOB

Summary

The successful management of a case of pulmonary oedema is described after the late recognition of an overdose of carbamazepine which complicated recognised benzodiazepine overdosage. The presentation and management are described and the possible mechanism of this rare complication discussed.

Key words

Drugs; carbamazepine.
Complications; pulmonary oedema.

Toxicity from ingestion of carbamazepine is uncommon. Few cases are described in the literature.[1–4] Cardiovascular dysfunction is the most common complication described, manifest usually as a prolongation of Q–T interval on electrocardiography (ECG) and supraventricular tachycardia. Neurological sequelae such as coma, respiratory depression, and dizziness have also been reported.

This report describes a case of massive intentional ingestion of carbamazepine and nitrazepam. The patient developed severe pulmonary oedema 48 hours after admission, and regained consciousness shortly before his sudden deterioration.

Case history

A 23-year-old male was admitted to the Accident and Emergency department in a comatose state. He had made two attempts at suicide in the preceding 2 weeks, and on this occasion was found unrousable at home by his family. He was flaccid, unresponsive to pain, and no reflexes could be demonstrated when he arrived at the Accident and Emergency department. His cardiovascular parameters were unremarkable apart from a sinus tachycardia of 120 beats/minute. His family believed that he had taken 26 tablets of nitrazepam 10 mg.

Tracheal intubation was achieved without the aid of drugs or relaxants. A large bore orogastric tube was passed; gastric lavage revealed some tablet debris. The patient was coughing at the end of the procedure and showed strong signs of protective reflexes to his airway. Consequently, he was extubated before admission to a general medical ward. The patient remained 'unconscious' for the next 36 hours before making purposeful responses to painful stimuli. Forty-seven hours after his admission he was a little more responsive but had a pyrexia of 38°C and crepitations were audible on auscultation of his chest. Fifty-seven hours after admission the patient was awake enough to answer simple questions, but his chest was deteriorating clinically and antibiotic treatment with intravenous amoxycillin was started to treat a presumed chest infection. He was transferred urgently to the intensive care unit (ICU) 4 hours later, after a rapid severe deterioration of respiratory function, with severe dyspnoea and cyanosis. Blood gas analysis revealed that the $P\text{a}O_2$ was 7.5 kPa and $P\text{a}CO_2$ 7.45 kPa while breathing 40% oxygen.

The patient arrived in the ICU in severe respiratory distress and had a respiratory arrest during transfer into bed. He was resuscitated immediately with 100% oxygen and his trachea was intubated, again without the aid of drugs. Pink frothy fluid was welling up the trachea and he demonstrated clinical signs of severe pulmonary oedema. Within 2 minutes, the patient's pulse could not be palpated and cardiac massage was started. The ECG revealed a supraventricular tachycardia of greater than 180/minute. The heart rate slowed to 150/minute after DC cardioversion, and the arterial pressure was 140/70 mmHg. Intermittent positive pressure ventilation (IPPV) with positive end expiratory pressure (PEEP) was started. Frusemide was given intravenously, and resulted in a diuresis of 400 ml/hour for the next 2 hours. Blood gas analysis (Table 1) revealed severe hypoxaemia.

The ventilation was adjusted by increasing the PEEP to 1.5 kPa and the minute volume was increased to 12 litres. This resulted in a slow improvement of gas exchange over the next 7 hours. The arterial pressure decreased initially to 75/50 mmHg, and the heart rate to 110 beats/minute.

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Table 1. Blood gas analysis, biochemical and haematological data after admission to the intensive care unit.

Time (hours)	0.5	1	7	18	42	45*	66	90
$F\text{IO}_2$	1.0	1.0	1.0	0.5	0.4	0.4	0.4	0.4
Positive end expiratory pressure (kPa)	0.5	0.5	1.5	1.5	0.5	0.5	0.5	0.5
$P\text{aO}_2$ (kPa)	4.9	5.9	22.1	25.8	13.4	6.1	28.0	21.9
Oxygen saturation (%)	54	73	99	99	98	81	99	99
$P\text{aCO}_2$ (kPa)	10.2	9.1	5.5	4.8	4.0	5.5	3.7	3.3
Urea (mmol/litre)	–	6.7	9.0	9.4	7.8	–	6.8	6.7
Total protein (g/litre)	–	71	–	56	58	–	–	58
albumin (g/litre)	–	35	–	27	27	–	–	28
globulin (g/litre)	–	36	–	29	31	–	–	30
Sodium (mmol/litre)	–	146	139	147	144	–	141	137
Haemoglobin (g/dlitre)	–	13.2	–	10.3	10.1	–	9.4	9.9
White cell count (× 10^9/litre)	–	15.3	–	10.8	8.7	–	7.3	6.2

* Spontaneous ventilation with continuous positive airways pressure.

Dobutamine 10 μg/kg/minute and dopamine 2 μg/kg/minute were started, and arterial pressure increased to 110/60 mmHg. A pulmonary flotation catheter was considered at this early stage, but the decision was deferred because of the initial tachycardia, and subsequent improvement.

The condition of the patient improved steadily over the next few hours. The inotropic support was withdrawn progressively 25 hours after admission to the ICU, and removed completely by 36 hours. The cardiovascular parameters at this time were: heart rate 90 beats/minute, arterial pressure 120/80 mmHg. Blood gases are shown in Table 1. IPPV was discontinued 44 hours after admission to ICU, and spontaneous breathing with continuous positive airways pressure (CPAP) was instituted. He remained pyrexial. The patient became distressed and hypoxaemic after less than 40 minutes and signs of pulmonary oedema reappeared. The $P\text{aO}_2$ decreased from 13.4 to 6.1 kPa, and $P\text{aCO}_2$ increased from 4.0 to 5.5 kPa. The decision was made to ventilate the lungs for a further 48 hours. The respiratory and cardiovascular parameters returned to their earlier values within 30 minutes. Shortly after this episode, we learnt that the toxicology investigations had revealed very high serum and urine concentrations of carbamazepine and no evidence of cocaine, heroin, or other drug abuse.

The patient's serum proteins were noted to be abnormally low (Table 1), with a serum albumin of 27 g/litre. Human plasma protein fraction was administered over the next 72 hours as it was presumed that a low plasma oncotic pressure and possible pulmonary capillary damage had contributed to the second episode of pulmonary oedema. Pulmonary artery catheterisation was considered again but deferred as the patient was now in a stable condition.

The patient's lungs were ventilated for a further 72 hours. The pyrexia settled within the next 24 hours. No positive bacteriological culture was identified at any time before or subsequent to antibiotic therapy. We feel in retrospect that infection was probably not a relevant feature of this patient's condition.

The patient was extremely difficult to sedate and required massive doses of fentanyl and midazolam. This was considered to be inappropriate in a patient who had taken an overdose. Sedation was achieved for the final 48 hours with an infusion of propofol 140 μg/kg/minute. This was entirely successful as a sedative and allowed rapid recovery of consciousness after termination of the infusion. The patient's urine turned bright green within a few hours of starting the propofol infusion. The green urine was fluorescent, and black precipitates were present. Blood biochemistry and physiological parameters were unaffected and the green colour disappeared within 48 hours of termination of the infusion. The event caused some concern amongst nursing staff and amused the patient's relatives.

The second attempt to wean the patient from IPPV was uneventful, and he was extubated one hour after stopping sedation. The serum proteins had returned to normal levels. He was discharged from the ICU to the ward, but absconded from the hospital to return home on the following day. A few days later, he repeated his overdose attempt, using the same drugs, but fortunately did not achieve the same toxic blood levels as before and did not require admission to ICU.

Discussion

Carbamazepine has been in clinical use for the last 25 years. It is used as an anti-epileptic and in the treatment of neuralgia. The drug is a carbamylated iminostilbene, related structurally to the tricyclic antidepressants.[2,5] Side effects of long-term administration include drowsiness, diplopia, dizziness, leucopaenia, hyponatraemia, and rarely, agranulocytosis.[5,6] Cases of heart failure have been reported in association with carbamazepine treatment.[7] Sinus tachycardia,[1,2] nodal bradycardia, first degree heart block, and ventricular ectopics have been recorded.[7] Neurological problems have also been documented.[2,3]

Pulmonary oedema has not been reported previously in cases of acute toxicity with carbamazepine, although relapse 45 hours after admission to hospital has been reported.[8] Our patient presented with a mild tachycardia but remained essentially stable for 61 hours before his cardiorespiratory collapse and gross pulmonary oedema.

Water intoxication as a result of carbamazepine treatment has been described.[9] We consider that it is reasonable to incriminate the overdosage of carbamazepine in the causation of his pulmonary oedema. Carbamazepine has a mild antidiuretic effect in conventional dosage, and has been used successfully to treat diabetes insipidus.[10] It is possible that the antidiuretic effect may be sufficient to produce pulmonary oedema in massive overdose. The patient's low serum proteins may be interpreted to support our theory. Unfortunately we do not have records of the blood levels of carbamazepine at any stage, nor an actual figure for urine levels, other than 'very high', because of the method of analysis.

Protracted absorption from altered bowel and gastric motility, and enterohepatic circulation, have been suggested to account for delay in collapse.[8] Our own patient presented in such a fashion that we were unaware of the true nature of his overdose until 4 days after the event. All cultures taken before administration of antibiotic treatment and subsequently, were negative. Viral and other studies were also negative. We believe that the overdose of carbamazepine is the most likely cause of his late cardiorespiratory collapse.

Green discoloration of urine after infusion of propofol for 3 days was reported recently.[11]

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Anaesthesia, 1988, Volume 43, pages 970–971

APPARATUS

Where there is no laryngoscope

B. P. O'DONOHOE, R. J. E. PAGE AND C. AWINI

Summary

In hospitals of the developing world where financial constraints limit the procurement of even the most basic medical equipment, improvisation has become important and necessary. We describe a reliable, low-cost, locally produced laryngoscope constructed out of wood.

Key words

Equipment; laryngoscope.

Laryngoscopy and intubation remain one of the cornerstones of safe anaesthesia. Unfortunately laryngoscopes are not always available in our locality or if they are, are all too frequently in a terminal state of repair. Several techniques describe laryngoscopy in the absence of a standard laryngoscope. These have included blind tactile oral intubation,[1] transillumination of the larynx with a torch together with laryngoscopy using a bent tablespoon, and a variety of locally improvised laryngoscopes.[2]

To ensure that laryngoscopy and intubation continue to be practised and taught in our region, to encourage the use of local materials and craftmanship and to promote a degree of self-sufficiency, a hand-carved, wooden laryngoscope was developed.

Description of laryngoscope

A compact one-piece design was favoured both for its simplicity and durability; the overall dimensions of the handle and adult curved blade were similar to that of a standard laryngoscope (Fig. 1). It was carved from the hardwood Odum which is readily available locally, with the grain in the long axis of the handle to give additional strength. A compartment to fit two standard U2 batteries was carved into the side of the handle, and secured by a lid fastened with two small screws (Fig. 2). The electrical connexions were constructed from workshop scraps and a simple on/off switch was mounted on the handle. The bulb was scavenged from an irreparable standard laryngoscope, although a normal torch bulb would provide satisfactory illumination. Finally, the laryngoscope was treated with a nontoxic wood sealant.

A straight bladed paediatric laryngoscope was constructed similarly (Fig. 3).

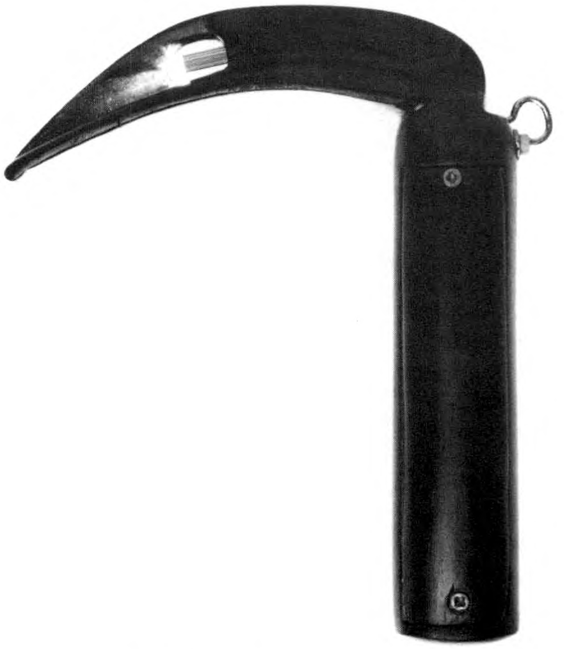

Fig. 1. The adult wooden laryngoscope.

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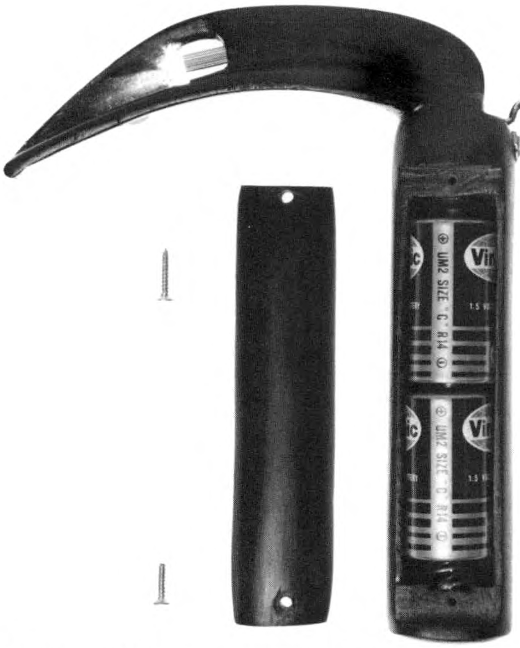

Fig. 2. The wooden laryngoscope showing the battery compartment.

These wooden laryngoscopes were reliable in clinical practice and as efficient as the standard metal version in providing a clear view of the larynx. The blade was cleaned satisfactorily with soap and water. The cost of £7, compared favourably with that of £72 for a standard adult metal laryngyscope or £27.50 for the plastic type,[3] and had the added advantage that it could be manufactured locally. To date there have been no problems with wood-boring insects!

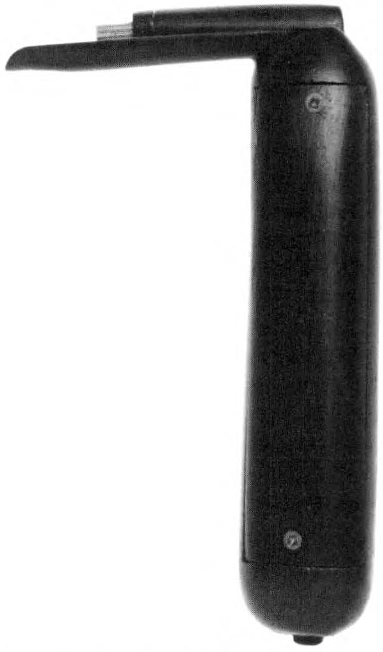

Fig. 3. A wooden straight bladed paediatric laryngoscope.

Acknowledgments

We thank Mr C. Diapi who carved the wooden laryngoscopes.

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HISTORICAL

The Alcock chloroform vaporizer

An early calibrated temperature-compensated plenum apparatus in its historical context

D. ZUCK

Summary

A long-forgotten chloroform inhaler, probably the first accurately calibrated, temperature compensatable, plenum vaporizer, is described. Its place in the dosimetric movement at the beginning of the 20th century is considered, together with a brief account of the life of its designer.

Key words

History; Nathaniel Henry Alcock.
Equipment; vaporizers.

A chloroform vaporizer unlike any that I was aware of was on display in the Museum of the Academy of Medicine in Toronto, Canada, during a visit I made in 1983. It was labelled simply as a chloroform inhaler of about 1915. Intriguingly it was of English make; the name and address of the manufacturer were stamped clearly on it and I felt that I ought to have known it.

Permission to photograph the apparatus was denied, but I was able to make a rough sketch. However, my attempts to identify it after my return home were unsuccessful; it did not appear in Bryn Thomas's *The development of anaesthetic apparatus*.[1] A search of the *British Medical Journal* and the *Lancet* from 1910 to 1920 was fruitless; nor was it illustrated in any of the contemporary textbooks of anaesthetics; and the manufacturer, C.F. Palmer, a well known instrument maker from whom our department had bought a drum recorder some 20 years earlier, seemed to have disappeared completely. But the apparatus continued to haunt me. It had certain features that one did not associate with that period.

Correspondence with the Curator on another subject at the beginning of 1987[2] encouraged me to ask again whether the apparatus might be photographed. I obtained as a result a number of colour transparencies, from which the accompanying illustrations have been prepared. Shortly afterwards, as a participant in the Second International Symposium on the History of Anaesthesia, I received a copy of a reprint of A. Goodman Levy's *Chloroform anaesthesia*, generously donated by a pharmaceutical company. I found in that remarkable book the first clue to the identity of the apparatus.[3] An urgent visit to the Wellcome Library to examine the relevant journal brought confirmation.

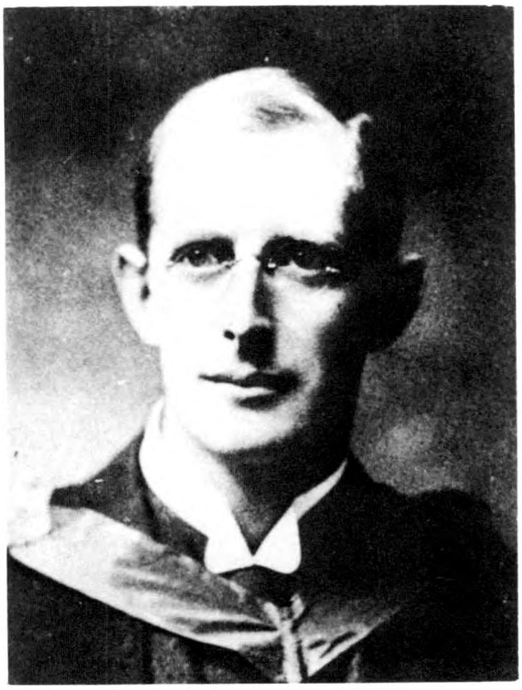

Fig. 1. Dr N.H. Alcock.

The designer—N.H. Alcock

The apparatus was designed by N.H. Alcock, MD (Fig. 1). Nathaniel Henry Alcock, son of Daniel Robert Alcock, assistant surgeon in the Royal Navy, was born at Dooen Glebe in the district of Letterkenny, Co. Donegal, on 12

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February 1871.[4] His uncle, the Rev. T.K. Abbott, was Senior Fellow of Trinity College, Dublin, and thus it followed that young Nathaniel studied there. He graduated in 1893 and obtained the BA with gold medal in natural sciences; he then proceeded with honours and prizes in various subjects to the degrees of MB, BCh, BOA and MD, in June 1896. He taught anatomy at Victoria University, Manchester, and physiology at Trinity College, Dublin, and then obtained a research appointment at the University of Marburg in 1902. He worked there under Professor Hans Horst Meyer (1853–1939), one of the leading pharmacologists of his time. Meyer and Overton had postulated independently the theory of the mechanism of narcotic action that now goes under their joint names.[5] Alcock kept up his interest in zoology during this time, and one of the fruits of his studies was a classic monograph on Irish bats.

Alcock was appointed demonstrator in physiology at the University of London in January 1903, in the new department where the chair had been created for A.D. Waller. Augustus Desiré Waller MD, FRS (1856–1922), the only son of the eminent physiologist Augustus Volney Waller who first described the degenerative nerve changes that now bear his name, was lecturer on physiology at St Mary's Hospital Medical School from 1886 to 1902. A.D. Waller was appointed director of the physiology research laboratory that the University of London had established in South Kensington in 1902. He had been the first to record the electrical activity of the heart, using a Lipmann capillary electrometer.[6] He was the author of a very successful textbook of physiology, in the dedication of which he lists his father's fundamental discoveries. His later investigations included the effects of narcotics and anaesthetics on nerve conduction, and this led him to consider the dangers of chloroform anaesthesia. His involvement in this is discussed later, but a full study of Waller's place in the history of anaesthesia has yet to be undertaken.

Alcock was appointed lecturer on physiology at St Mary's Hospital Medical School in January 1904, the post previously held by Waller, and the following year he married Nora, daughter of Sir John Scott, KCMG. His son (Dr N.S. Alcock, personal communication) thinks she may have been working in Waller's laboratory when they met. Waller himself had married one of his own medical students, Miss Palmer, as is well known.[7]

Alcock became Vice-Dean of the medical school in 1906. He approached the Board of Education in this capacity, when St Mary's faced a severe financial crisis, and was able to establish for the first time that medicine be regarded as a science and that medical schools be eligible for Government grants. He was able to place St Mary's on a much more secure financial footing as a result, and a number of other medical schools soon followed his example, with equal benefit. This achievement brought him to the wide notice of the profession.

The Alcock Apparatus

Alcock designed his apparatus (Fig. 2), and published a description of it, in 1908.[8] His purpose was two-fold. He wished to investigate whether the results of the many experiments on the actions of known percentages of chloroform on animals were equally applicable to man, and he hoped to reduce 'the disadvantages that are inseparable from the administration of an active drug in unmeasured quantities.'

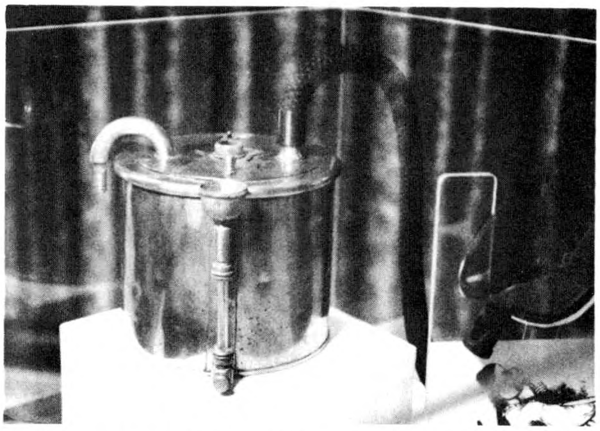


Fig. 2. The Alcock Chloroform Inhaler.

His description of his vaporizer is brief and modest. 'The apparatus consists of a circular copper vessel 5 in. in diameter and 4½ in. deep, which contains 150 c.cm. of chloroform; 1¼ in. from the bottom is fixed a shelf closed except for two oblong holes. Immediately above and touching this shelf is a circular plate, movable by means of a hollow rod in the centre, and pierced by two triangular apertures. These can be adjusted by the centre rod so as to expose more or less of the fixed oblong holes in the shelf and so produce greater or smaller openings into the space below. Air (supplied from a small foot bellows) enters the chamber by one tube opposite one aperture, and leaves by another tube, taking up more or less chloroform vapour according to the size of the apertures. A thermometer in the hollow rod indicates the temperature of the chloroform below, and a water jacket surrounding the chamber serves to keep the temperature between certain limits.'

Alcock calibrated and tested the apparatus using the densimetric method of Waller and Geets, which was the precursor of the better-known chloroform balance.[9] Variations in the temperature of the chloroform could be corrected within 0.1% error between 60° and 70°F by sliding the percentage scale against the index pointer (Fig. 3); even between 55° and 75°F the additional error at the extreme ends of the scale did not exceed 0.2%. It was claimed also that the concentration was independent of shaking; this would imply that the mixture always left the vaporizing

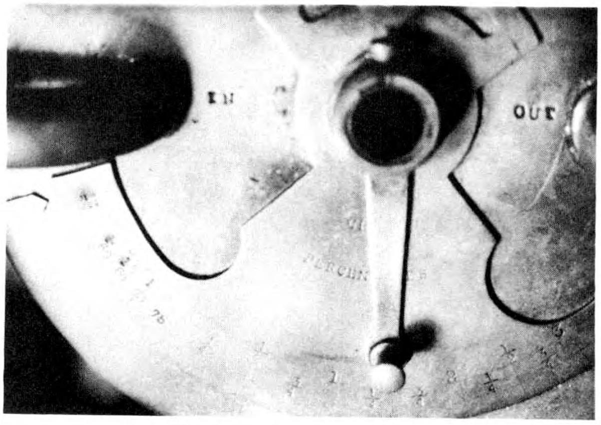


Fig. 3. The percentage scale.

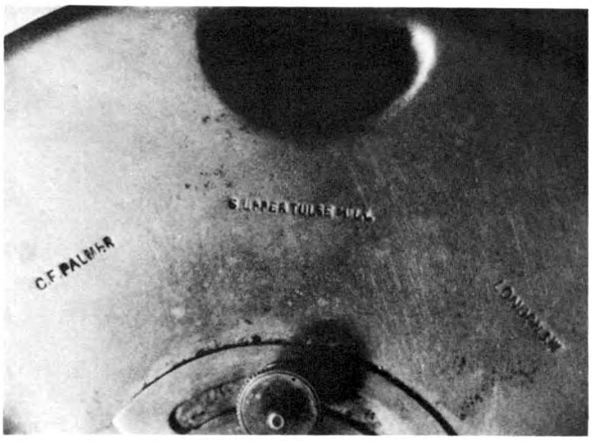


Fig. 4. The manufacturer—C.F. Palmer, 6 Upper Tulse Hill, London SW.

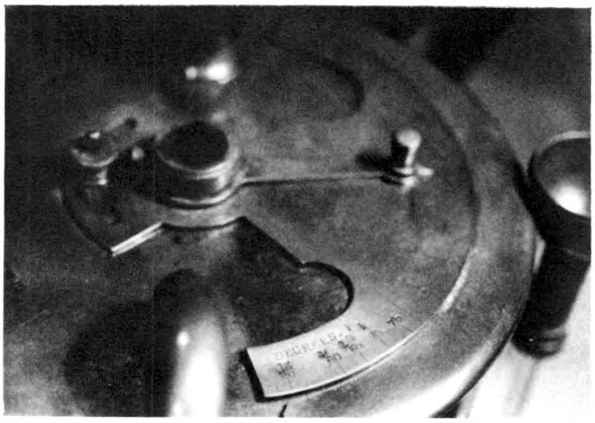


Fig. 6. Lower end of scale—temperature calibration in degrees Fahrenheit.

chamber fully saturated. The claim was of some significance, as will be seen. Alcock thought that the apparatus was sufficiently portable to be used by the general practitioner, 'and as the air supply is given from a foot bellows, leaving both hands free, it is quite feasible for one man to use the machine by himself if need be.' The alternative source of air was an electric fan. Alcock concluded by expressing his appreciation to the manufacturer, C.F. Palmer (Fig. 4), for many useful practical suggestions.[10]

It is, then, a calibrated plenum vaporizer with a facility for temperature compensation. The vaporizing chamber rests in a water jacket; this accounts for the difference between the dimensions given by Alcock and those recorded in the Toronto catalogue.[11] Alcock's description fails to indicate the appearance of the apparatus. It is colourful; made of a warm glowing copper and the breathing tube is covered with a finely woven, finely chequered, red and black fabric; the facemask is a translucent amber. The filling arrangement is quite elaborate, with a glass tube to indicate the contents, and a drainage device. There is a percentage scale and a pointer (Fig. 5). There are temperature calibrations, at the lower end of this scale, from 55° to 75°F (Fig. 6). In use the temperature of the chloroform was read on the thermometer, and the appropriate graduation on the temperature scale was lined up against the index. This corrected for temperature variations between 60° and 70°F within a limit of 0.1% error, and 0.2% outside that range. The scale indicates that the water started at room temperature or a little warmer. The percentage scale is calibrated in 0.25% intervals from zero to 3.5%. The word 'dangerous' is engraved at the top end of the scale (Fig. 7).

The chloroform–air mixture was delivered through the flexometallic fabric covered tube to the facemask with integral expiratory valve. The facemask may be made of celluloid, which had been used to construct transparent anaesthetic masks at about this time. Celluloid, a nitrated cellulose, was an early plastic widely used in the manufacture of children's toys, especially dolls; its use was banned in about the late 1930s because it was explosively inflammable.

Alcock's description of the mechanism may have been incomplete; it is difficult to see exactly how temperature compensation could have been effected, and how the splitting ratio was achieved.

Alcock mentioned that the apparatus was used to make observations on the effects of the administration of known percentages of chloroform. These were reported at a meeting of the newly formed Section of Anaesthetics of the Royal Society of Medicine on 9 December 1908.[12] Alcock commenced, 'The theory and practice of anaesthesia are too often spoken of as distinct and even antagonistic entities. This view is founded on a misconception, and theory is based on practice and on that alone.' If observed facts are not accounted for by the theory, it is the theory that is at fault. 'It is, perhaps, a truism to say that our knowledge of any subject is in direct proportion to the accuracy with which exact measurement can be applied to it.' Measure-

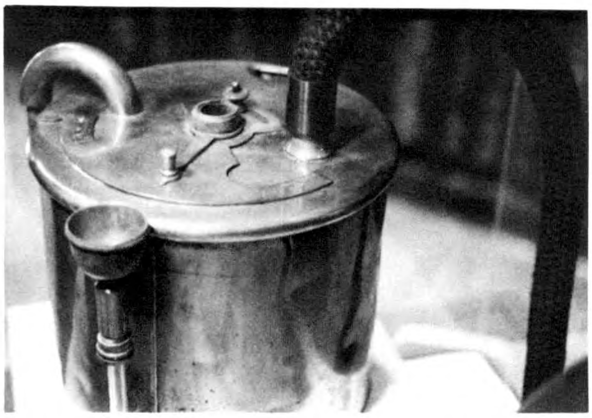


Fig. 5. General arrangement of percentage and temperature controls.

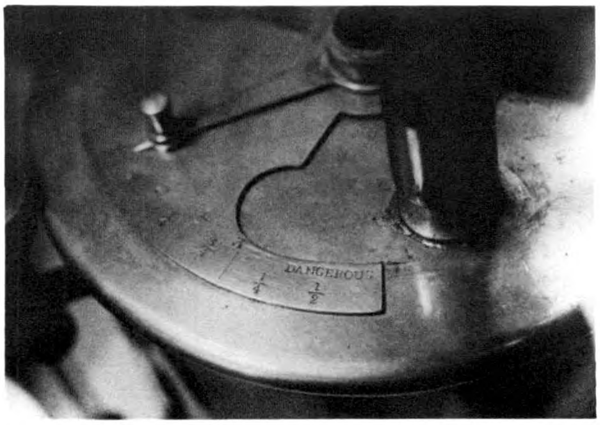


Fig. 7. Upper end of scale—3.5% chloroform is DANGEROUS.

ment in anaesthetics is often difficult and sometimes impossible. 'But the ideal should always be kept in mind, and one should not feel satisfied with our knowledge of anaesthesia until we are able to predict exactly what effect will follow from the inhalation and absorption of a known quantity of the drug employed.' He proposed to measure only the percentage in the inspired air, not the amount absorbed nor its fate in the body, and in justification of this limited scope he pointed out that this is the only factor that is under the direct control of the anaesthetist, and is the immediate cause of all the effects produced.

He gave a brief description of his vaporizer, but did not mention temperature compensation. He compared it with the 'vacuum' or drawover apparatuses of Snow, Harcourt, and Levy, which were compact but introduced some obstruction to free respiration, and the so-called 'plenum' system used by Dubois, Waller, and Rŏth-Drager (*sic*), which he preferred.[13] The final design was adopted after a long series of trials. Air was supplied by a foot bellows, but an electric fan could be used. He paid great attention to ensuring the accuracy and reliability of his vaporizer under actual conditions of surgical anaesthesia, and described the method of calibration in more detail than in his earlier account. He used the densimetric method of Waller and Geets, which Levy had shown gave practically identical results to the combustion method of Vernon Harcourt, to show that the maximum calibration error under ordinary conditions did not exceed 0.1%. Repeated determinations showed that the usual variation was 0.1% or less. Variations in the air supply between 8.5 and 20 litres/minute had no effect; the percentage of chloroform remained practically constant. Below 8 litres the percentage decreased, so no harm was done. Certain features of the apparatus seem to have been derived from A.G. Levy's regulating chloroform inhaler of 1905, and Alcock makes a very perceptive comment that indicates that it is to Levy that we owe the modern concept of vaporizer design.[14] The usual air supply was between 16 and 20 litres/minute. It should be noted that neither of Alcock's descriptions of his apparatus contained any illustrations; it is perhaps because of this that it is virtually unknown today, and was so difficult to identify.[15]

Alcock then reported the results of the study of the effects of known percentages of chloroform on 50 patients. The anaesthetists were Drs Blumfeld, Beaumont, and Collum, of St Mary's Hospital. The usual clinical signs of depth of anaesthesia seem to have been employed, and the corneal reflex is mentioned in particular. The percentage inhaled was noted carefully and plotted against time on squared paper. Ten such plots are reproduced in the publication (Fig. 8). They demonstrate the concentration required for induction and maintenance of anaesthesia in patients of different build, age, degree of nervousness, and so on. They

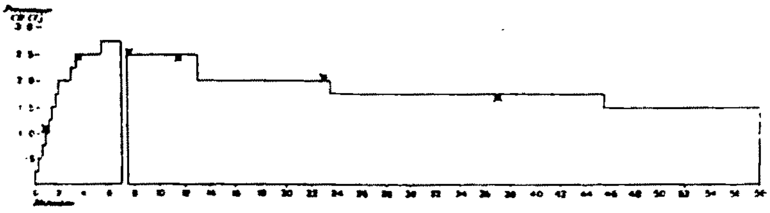


Fig. 2.

Case 33.—Male, aged 9; undescended testicle (Dr. Beaumont and Mr. Collier); October 9, 1908; the crosses mark estimations on October 16 in laboratory. Meth. CHCl₄.

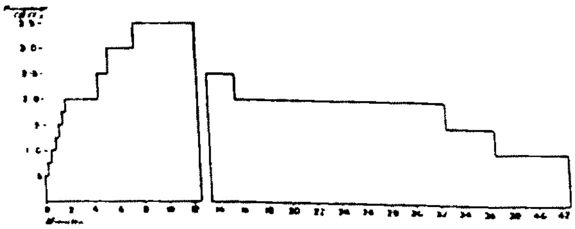


Fig. 6.

(Case 16.—Female, aged 30; appendicitis (Dr. Beaumont and Mr. Clayton-Greene); stout patient; August 14, 1908

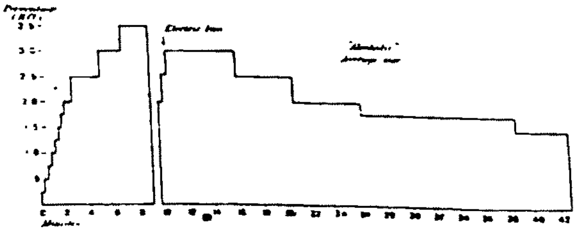


Fig. 7.

Case 29.—Male, aged 45; ventral hernia (Dr. Beaumont and Mr. Lane); October 8. 1908. Ac. $CHCl_3$ (H_2O in $CHCl_3$). 80 c.c. used.

Fig. 8. Alcock's anaesthetic charts—the percentage of chloroform is plotted against the duration of administration.

are the precursors of the plots that we draw, perhaps sometimes less precisely, on our anaesthetic records today.

The average induction time was 8–9 minutes and up to 3% of chloroform was needed. The break in the chart indicated the move from the anaesthetic room to the operating theatre and hence the duration of induction. It was possible in general to reduce the concentration progressively during the operation. The amount of chloroform vaporized averaged about 1 cc/minute and for ordinary healthy adults the anaesthetic charts showed great similarity.

Attention was then directed to the effects of age, build, alcoholism, and the type of operation. Conclusions could be drawn only tentatively, because the groups were small. Young children seemed to require less chloroform. Fat people took more than thin, as did alcoholics; in one case even the maximum of 3.5% delivered by the apparatus was insufficient and it was necessary to revert to the open method. The duration and severity of stimulation, as regards the operation, were significant. Animal experiments had confirmed the clinical observation that intense stimulation such as pulling on the parietal peritoneum would restore the just absent corneal reflex, and also cause quickening and increased depth of respiration and a decrease of arterial blood pressure. This is the only occasion when blood pressure is mentioned; obviously it was not measured in the operating theatre.

Alcock drew the conclusion that anaesthesia with known percentages of vapour was at least as easy and certain as by the ordinary method. During induction the concentration should rise by steps of 0.25% every 0.25 of a minute until 2% is reached in 2 minutes; thereafter the increase should be slower, to 2.5% in 3 minutes, and 3% in 5 minutes if necessary. Two percent is usually ample when induction is complete; reduced gradually to 1% after 25 minutes. Individual variations occur, and with due allowance for these it is legitimate to apply the conclusions deduced from experiments on animals to the human subject.

Dr Blumfeld, in the ensuing discussion, was most enthusiastic about the apparatus *per se*. It gave most excellent results. The experienced anaesthetist would find an enormous saving of labour. 'But that saving of labour for the anaesthetist meant a good deal of extra labour in other directions. In a hospital theatre such a machine was of immense value, but outside he feared it was not. If each anaesthetist could be supplied with a boy to work the bellows, or with an electric fan, or with a motor-car to carry the boy, the machine, and the fan, conditions would be about ideal, and he would always take Dr Alcock's apparatus with him.' In hospital, however, it was a great advantage to have such an instrument, from the teaching as well as the practical aspect; both were included in the anaesthetist's work. He thought every hospital should have an inhaler of this pattern, in order that students might learn something about the percentage of chloroform vapour required to produce the different stages of anaesthesia in varying types of patients.

Dr Collum reported a postoperative death in an already comatose patient with a suspected cerebellar tumour whom he had not wanted to anaesthetise. He did not think the apparatus had anything to do with the death. 'The apparatus was exceedingly interesting and it was scientific, but there was rather a lot of it, and he had already mentioned the inconvenience arising from the noise it made. And unless one had a laboratory boy to work the bellows, an electric fan was needed: he had seen the boy looking very sorry for himself after a couple of hours at the bellows in the summer time. He was certain the general practitioner would not carry it to his cases in the country if he had to travel on a bicycle ... Dr Blumfeld said it was a useful instrument to have in hospital for teaching students; but what was the use of teaching students what they would not be likely to use? ... Therefore, though he thought the apparatus a valuable one, he did not see that it had a very wide field of utility.' He wondered about its accuracy; while he would have confidence in an instrument passed by Dr Alcock, how would he know if one bought from an instrument manufacturer was up to standard?

Dr A.G. Levy congratulated Dr Alcock upon the success of his inhaler, on its extreme simplicity, and on the scientific and clear way in which he had brought the subject before the Section. Alcock, in his reply, thought his apparatus could be made more portable. In his opinion the class of person for whom it would be of most service was the country practitioner who had about 30 cases of anaesthesia a year. 'He often was short-handed and was out of practice with anaesthetics, and the trouble in carrying the apparatus about would be more than compensated for by the ease and certainty with which the anaesthetic could be administered.' As regards noise, the present bellows was almost silent. Machines supplied commercially were carefully regulated. He had tested several at random and they were surprisingly accurate. He had used oxygen instead of air in one test case, with manifest benefit: an old lady, very fat, known to have a fatty heart, with gallstones. 'He was told that if he succeeded in anaesthetising her, and she was safely got off the table, the machine might be regarded as a success.' She came round in the usual time at the end of the operation and her pulse was better than before. 'Where there was a suspicion of cardiac failure, he thought that was the way to attempt to prevent difficulties.'[16]

It was reported[17] that a number of specimens of the inhaler, of various sizes and patterns, were shown. One was fitted with a foot-bellows, one with an electric motor to drive the air through the chloroform chamber, and one with an oxygen cylinder. The apparatus was also shown in section, so that the inner working of the instrument could be more thoroughly understood. Dr Alcock's presentation was illustrated by numerous lantern slides.[18]

Discussion

No single feature of Alcock's vaporizer was original. There had been plenum vaporizers before, although the name had only recently been applied to them. Buxton had added foot bellows to Junker's inhaler in 1888. The water jacket dated back to Snow's first ether inhaler, and in a more complete form had been adopted by Levy, whose drawover chloroform vaporizer also had the facility of temperature compensation. The anaesthetist read the temperature of the chloroform on a partly-immersed thermometer, and adjusted the pointer to the appropriate isotherm on the percentage scale.[19] But Alcock's apparatus was the first to incorporate all these features: the first plenum vaporizer with a water jacket, calibrated, temperature compensated, and accurate to 0.1% over a wide range of flow. The whole was more than the sum of its parts.

Alcock's research was in line with contemporary interest. Concern about the deaths and morbidity associated with chloroform anaesthesia dated back almost to the time of its introduction, and had been the subject of a number of committees of enquiry.[20] Waller's public involvement with the problem began in 1897. Early next year he spoke on chloroform at a meeting of the Society of Anaesthetists, emphasising its potency and the importance of awareness of the dosage administered.[21] He published a letter in 1901 that was strongly critical of the report of a British Medical Association (BMA) Anaesthetics Committee. He set out a programme of research in it, the fourth requirement of which was 'a careful redetermination of the . . . percentage of chloroform required for various degrees of anaesthesia . . .' In 1901 also he persuaded the BMA to fund research on chloroform, to be carried out at the physiological laboratory of St Mary's Hospital Medical School. There can be little doubt that Alcock's vaporizer, and his investigations, were aimed at fulfilling part of Waller's research programme. The BMA appointed a new Chloroform Committee in July of the same year, with Waller at its head, and the anaesthetist Dudley Buxton, as its secretary. It immediately coopted the physical chemist A.G.V. Harcourt, who had devised a combustion method of estimating the amount of chloroform in air.[22]

Harcourt undertook the task of designing a safe inhaler, and this was described in 1903.[23] Unfortunately Waller appears to have resigned from the Chloroform Committee about 1904, when the Committee declined to publish a report highly critical of Harcourt's inhaler. Waller had found that, when shaken, as might happen during induction in a restless patient, the Harcourt inhaler could deliver a percentage up to five times the nominal value; and he strongly advocated the use of plenum apparatuses, rather than drawover.[24] So the Committee's final report, issued in 1910, was coloured by the enthusiasms of others.[25]

Of the 14 regulating inhalers that were considered by the Committee, only two incorporated a calibrated, temperature-compensated scale. These were Alcock's, a plenum apparatus, and Levy's, a drawover. Alcock's had the advantage that oxygen could be added to the inspired mixture without upsetting the calibration. Among the others, Junker's was uncalibrated and unpredictable. Roth-Dräger's was a mechanised drop-bottle, Waller's chloroform balance, on his own admission, was more of a laboratory apparatus, and Harcourt's, as Waller had shown, was not entirely reliable and depended for its temperature compensation on the warm hand of the anaesthetist. Yet it was Harcourt's that the Committee favoured. It had the essential virtues of 'simplicity, exactness, and portability', and that 'the mixture of air and chloroform is automatically limited to a maximum of 2 per cent',

Of Alcock's apparatus the Committee recognised that 'A series of successful applications of this inhaler for surgical work has been recorded . . . and as it has been used with considerable success in hospital practice, may be described fully.' There followed a description taken from that published by Alcock himself. However, it was a plenum apparatus, and in the eyes of the Committee it suffered from all the drawbacks of these, complexity and lack of portability. Alcock's statement that 3% chloroform in air may be used safely during induction provided due care is exercised was criticised as a contradiction in terms. The concluding comment was that 'The apparatus tested clinically appears to have been a success as far as the present experience gained with those patients upon whom it was tried permit us to arrive at any definite judgement.' It is evident that no member of the Committee had used the apparatus himself, and so it was dismissed, damned with the faintest of labyrinthine praise. Dr Boulton has pointed out that not until the 1950s did the calibrated temperature-compensated plenum vaporizer become a feature of anaesthetic machines.[26]

What did his contemporaries think of it? Blumfeld wrote, 'Vernon Harcourt's inhaler . . . and the more cumbrous "plenum" inhalers (Waller, Dubois, etc.) are invaluable for teaching the importance of dosimetric administration. When this principle has been mastered, the student should learn how to meet its demands by the simpler methods described in the text.'[27] But why guess, when a measuring device is to hand?

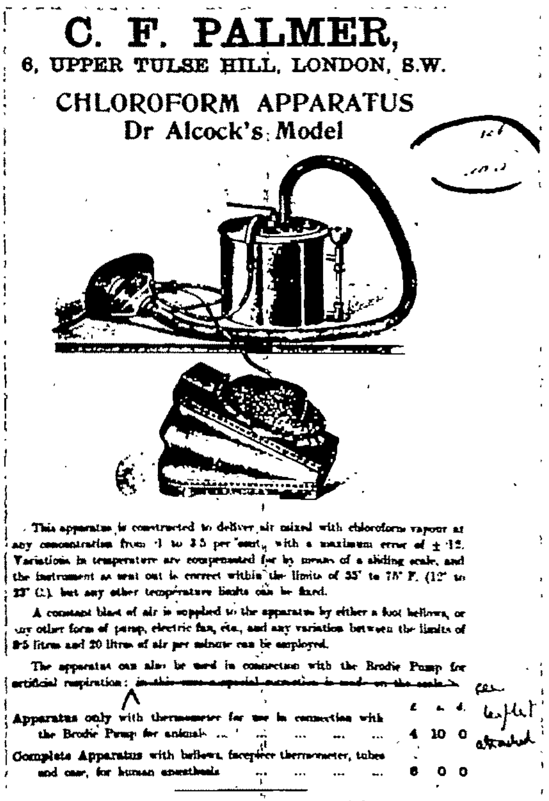
Hewitt virtually reproduced Alcock's own description and his views on induction techniques. There is no indication that he had used the apparatus himself.[28] Blomfield, later in his major textbook, claimed rather unfairly, that the first accurate vaporizers were designed by physiologists since it was they who were doing the lethal experiments! The truth is that they were virtually the only people doing any experiments at all. He also mentioned, having missed the point of the principle on which Levy's definitive apparatus was based, that among the disadvantages of drawover apparatuses was that the amount of chloroform vaporized depended on the patient's tidal volume, and that most of them could not provide more than 2%. But he still thought that plenum inhalers were too bulky.[29]

The reasons why Alcock's vaporizer, with all the advantages that it appears to us today to offer, did not become popular with contemporary anaesthetists, will have become clear from the preceding discussion. Most clinical anaesthetists considered there was no great need for a dosimetric method of administration. But their need, in the prevailing conditions of anaesthetic practice for portability of equipment, comes through strongly. A small number of anaesthetists received a modest stipend, but all specialists in hospital practice depended on private work to make a decent living; and that entailed travel. Portability was more important than accuracy to the peripatetic jobbing anaesthetist of the Edwardian era.

Nevertheless, Alcock's apparatus was marketed by Palmer (Fig. 9), and seems to have achieved some acceptability in hospital practice. It was chosen by Morriston Davies as the anaesthetic vaporizer to be incorporated into his remarkable positive pressure apparatus, designed in 1911, to facilitate open chest surgery, 'and it has proved itself to be most satisfactory'.[30] According to Levy, 'Alcock's *ad plenum* inhaler is compact and simple in construction, and it would appear that some such apparatus as this most nearly approaches what is required . . . This apparatus should be adjusted for a higher rate of delivery than 20 litres/minute, and the temperature correction should be extended to wider limits; it should then be efficient for the great majority of cases.'[31]

Alcock's later career

Alcock was awarded the degree of DSc in 1909 by the University of London for his physiological researches. In the same year he published with his colleague F.O'B. Ellison his *A textbook of experimental physiology*, with a commendatory introduction by Professor E.H. Starling,



C. F. PALMER,
6, UPPER TULSE HILL, LONDON, S.W.

CHLOROFORM APPARATUS
Dr Alcock's Model

This apparatus is constructed to deliver air mixed with chloroform vapour at any concentration from ·1 to 3·5 per cent., with a maximum error of ± ·12. Variations in temperature are compensated for by means of a sliding scale, and the instrument as sent out is correct within the limits of 55° to 75° F. (12° to 23° C.), but any other temperature limits can be fixed.

A constant blast of air is supplied to the apparatus by either a foot bellows, or any other form of pump, electric fan, etc., and any variation between the limits of 0·5 litres and 20 litres of air per minute can be employed.

The apparatus can also be used in connection with the Brodie Pump for artificial respiration: ~~in this case a special correction is used on the scale.~~ see leaflet attached

	£	s.	d.
Apparatus only with thermometer for use in connection with the Brodie Pump for animals	4	10	0
Complete Apparatus with bellows, facepiece thermometer, tubes and case, for human anaesthesia	6	0	0

C. F. PALMER, 6, UPPER TULSE HILL, LONDON, S.W.

Fig. 9. C.F. Palmer's trade leaflet.

FRS. The book was very well received, the reviewer regretted only that 'The great obstruction to a proper course in physiology has been, and still is, the legal restrictions which prevent the student from learning on the lower animals the routine of the administration of anaesthetics or the techniques of the simple operative procedures necessary for the investigations of the functions of the body. The British student hitherto has been compelled to gain his first experience in giving anaesthetics and in operation on man himself . . . in the United States the medical students carry out a proper course of investigations of blood pressure, respiration, etc., on fully anaesthetised animals, and this course forms one of the most fundamentally important in their whole curriculum.'[32] One wonders to what extent this restriction of the education of the British medical student was responsible for the failure of British anaesthetics to develop in line with that of the United States before the Second World War.

Alcock was living at this time at 22 Downshire Hill, on the edge of Hampstead Heath. His salary of £400 per annum was supplemented by his work as an examiner for the Royal College of Physicians and the National University of Ireland to the extent of an additional £300. He was head of a substantial, well-equipped laboratory, and was the author of some 10 significant publications, which included work on the mechanism of nerve conduction. Several of those who had worked under him had achieved professional advancement. Dr B.J. Collingwood, who had researched on chloroform, was now professor at the National University, Dublin; Dr Ellison was a candidate for the chair of physiology at the University of Capetown; Dr Mansfeld was Privat-Docent at the University of Budapest; and Mr G. Roche Lynch was embarking on a career in forensic pathology.[33] Alcock was active in the affairs of the British Association for the Advancement of Science; he had been one of the secretaries of the Section of Physiology in 1907, when Waller had been President. In 1909 the annual meeting was held in Winnipeg. Starling was President of the Section, Waller one of the Vice-Presidents, and Alcock the secretary and recorder; Waller and Alcock travelled to Winnipeg together.[34] A large part of the business of the Section of Physiology was devoted to anaesthetics.[35] Waller described and demonstrated his chloroform balance and Alcock demonstrated his inhaler. They then continued to the University of California, Berkeley, where Waller delivered the Hitchcock Lectures.[36]

Alcock was elected to the chair of physiology at McGill University, Montreal, in 1911, but he held this post only for 2 years. He died on 13 June 1913 at the age of 42. Sir William Osler wrote: 'The death of Dr Alcock is a great loss to the Faculty of Medicine . . . The energy and enthusiasm he displayed, though suffering for nearly 3 years from medullary leukaemia, were remarkable.' Other obituarists mentioned his great breadth of scientific interest, likening him to the great von Helmholtz. He was said to have a charming and humorous personality, flavoured with a healthy satirical tendency which could not always be quite suppressed in his writings. '. . . a pleasanter colleague one could never meet.'[37]

Apart from his work on chloroform, among his more important contributions were publications in the *Journal of Physiology* and in the *Proceedings of the Royal Society* on the physical, chemical, and electrical properties of nerves, on fatigue in nerve, and on the velocity of conduction of the nerve impulse.

The family returned to the United Kingdom after his death, and in recognition of Professor Alcock's contribution to medical education the Prime Minister, Mr Asquith, granted Mrs Alcock the unusual distinction of a pension out of the Civil Service Fund.

Acknowledgments

Apart from those whose help is acknowledged in the notes and references, I am grateful to: my brother, Dr J. Zuck, for the photographs of the apparatus; Professor D.R. Bevan and Miss M. Pacelli, Department of Anaesthesia, McGill University, Montreal, for the photograph of Professor Alcock and other helpful information; Mr A. Brooks of the Ontario Science Centre; Dr A.B. Davis, Curator, Medical Sciences, Smithsonian Institution, Washington DC; Mrs F. Nowell-Smith, Curator, Academy of Medicine, Toronto; Mr N. Palmer, Librarian, St Mary's Hospital Medical School; Miss L. Ward, Research Assistant, Wellcome Museum of the History of Medicine at the Science Museum, South Kensington; the staffs of the Wellcome Library and of the Library of the Royal College of Surgeons of England; Dr R. Westhorpe, Curator, The Geoffrey Kaye Museum of Anaesthetic History, Melbourne, Australia; Mrs M. Butler, Medical Librarian, and Mr M. Moor, Medical Photographer, Chase Farm Hospital, Enfield; and my secretary, Miss E. Massen.

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10. Charles Fielding Palmer was a scientific instrument manufacturer who specialised in 'one-offs'. He built up a clientèle by visiting research laboratories and finding out their requirements. He seems to have been to physiologists what Charles King was to anaesthetists. The firm moved from Tulse Hill to Sheerness after a fire in the early 1930s. The earliest catalogues extant are for 1934, and since these are held both by the Science Museum South Kensington, and the firm itself, it is likely that these were the earliest produced. It has been suggested that before this only individual product leaflets were printed. C.F. Palmer became one of the main producers of kymographs in the UK. The firm survives as Palmer Bioscience, a subsidiary of Baird and Tatlock, who marketed their products from the early part of the century, and it now manufactures electronic physiological recording equipment. C.F. Palmer himself is thought to have died in the late 1950s or early 1960s. I am grateful to Mr T. Cook of Palmer Bioscience for much of this detail. He is researching the history of the Company and would welcome any further information.
11. The Toronto catalogue registration data sheet describes the apparatus as a circular metal canister 14.1 cm (5½ in.) high, and 16.6 cm (6½ in.) diameter at the base. Engraved on the top of the canister are the following:

    C.F. Palmer, 5 Upper Tulse Hill, London S.W. (Fig. 4)
    $CHCl_3$ PERCENTAGE (Fig. 3) but partly obscured by the pointer.
    IN OUT (against the inlet and outlet ports)

    The vaporizer is accompanied by a bellows, a plastic mask, a corrugated metal tube with fabric cover 71.1 cm (28 in.) long, and a thin corrugated tube 155.5 cm (61¼ in.) long. The whole is contained in a mahogany box. It was acquired by the museum in October 1969 from the Department of Physiology of the University of Toronto.
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13. According to the OED the use of *plenum* in the sense of a space full of matter dates back to 1678. The present usage dates from 1903, when the term first described a system for the artificial ventilation of buildings, but the name was soon applied to one type of vaporizer. Levy uses the expression *ad plenum.*
14. Alcock (p. 19) points out that it is to Levy that we owe the concept of the splitting ratio in the design of anaesthetic vaporizers. See Zuck D. The development of the anaesthetic vaporizer—the contribution of A. G. Levy. *Anaesthesia* 1988; **43:** 773–5.
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32. Book review. *British Medical Journal* 1910; **i:** 1358–9.
33. All this information is derived from the copy of Alcock's *curriculum vitae* submitted to the University of London in 1910. I am grateful to Mrs L. Atkinson, Librarian, Unversity Laboratory of Physiology, Oxford, for a copy of this document, and for the Palmer trade leaflet, which reveals that the stem of the thermometer was at right angles to the bulb.
34. Dr N.S. Alcock informed me that he still has the series of picture postcards that his father sent from all the places he stopped at on the journey from Montreal to California. The Alcock and Waller families were on very friendly terms, and

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Forum

Hypoxaemia during induction of anaesthesia—an audit of children who underwent general anaesthesia for routine elective surgery

G.J.A. Laycock, BM, FFARCS, DCH, DRCOG, Registrar, L.R. McNicol, MB, ChB, FFARCS, Consultant, Department of Anaesthetics, Royal Hospital for Sick Children, Yorkhill, Glasgow, G3 8SJ.

Summary

Arterial oxygen saturation was measured using pulse oximetry during induction of anaesthesia in 108 children aged 10 days–14 years. No restriction was placed on the method of induction. Oxygen saturation decreased to less than 90% in 29 children (26.8%) and less than 80% in seven children (6.4%). There was a significantly increased incidence of desaturation (to less than 90%) in children under one year of age, in those who had no premedication, in those who received only atropine as a premidicant and in children who were anxious or crying before intravenous induction. Oxygen saturation did not decrease below 90% in any child who received inhalational induction.

Key words

Anaesthesia; paediatric.
Monitoring; pulse oximetry.

Induction of anaesthesia is known to be associated with a risk of hypoxaemia. Rapid changes in alveolar gas tensions occur even in a smooth transition from the awake to the anaesthetised state.[1] Other factors such as airway obstruction, respiratory depression and difficulty with tracheal intubation may interfere with ventilation and precipitate a decrease in arterial oxygen saturation (SaO_2). Previous studies in adults have demonstrated that SaO_2 may decrease to 75% during tracheal intubation after induction of anaesthesia with thiopentone and suxamethonium in patients who breathe air.[2] Increased age and poor preoperative condition also result in an increased incidence of hypoxaemia[3] at induction.

There is little information about hypoxaemia in children, partly because of difficulties in monitoring arterial blood gases. The availability of pulse oximetry has provided a means of continuous, reliable and noninvasive monitoring of SaO_2.[4] The purpose of the present study was to measure SaO_2 during induction of anaesthesia in children scheduled to undergo routine elective surgery. No restrictions were placed on the type of premedication or method of induction used. Frequency and severity of hypoxaemia were recorded together with factors associated with significant decreases in SaO_2.

Patients and methods

Arterial oxygen saturation was measured in 108 children who underwent general anaesthesia. The patients were selected at random from routine lists and were anaesthetised either by a registrar, senior registrar or consultant. The anaesthetists were aware of the purpose of the study but were unable to observe the oximeter display during induction. The anaesthetic technique was not influenced by the presence of the observer (G.J.A.L.) who recorded all the observations.

The pre-induction condition of the child was assessed on a four-point scale in the anaesthetic room (Table 1). Concurrently the oximeter probe was sited and a baseline SaO_2 obtained; the finger probe was used in children and the foot probe in babies. SaO_2 was then observed continuously during induction of anaesthesia. The maximum decrease in SaO_2 was recorded together with the time taken to return to the baseline value. All measurements were made with a Biox 3700 pulse oximeter. Six categories of induction method were used (Table 2). No child was pre-oxygenated, but the lungs were ventilated artificially before tracheal intubation (except awake intubation). A minimum inspired oxygen concentration of 33% was used in all children except those in the intravenous/air group.

The correlation coefficient and the Mann–Whitney *U* test was used to express the results of continuous variables and the Chi-squared test for discrete variables. A p value of less than 0.05 was considered to indicate statistical significance.

Table 1. Assessment of pre-induction state of children in study.

1, Asleep or heavily sedated
2, Awake and cooperative
3, Awake and fretful
4, Screaming and uncomfortable

Table 2. Methods of induction of anaesthesia.

Intravenous, spontaneous ventilation through facemask
Intravenous, oral intubation
Intravenous, nasal intubation
Intravenous, plus supplemented intravenous agent, air
Awake intubation
Inhalational induction

Correspondence should be addressed to Dr L.R. McNicol please.
Accepted 26 April 1988.

0003–2409/88/110981 + 07 $03.00/0

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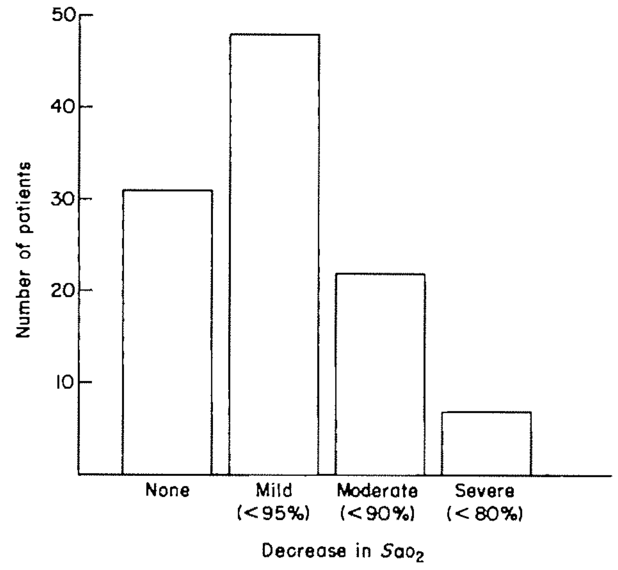

Fig. 1. Maximum fall in Sao_2 during induction.

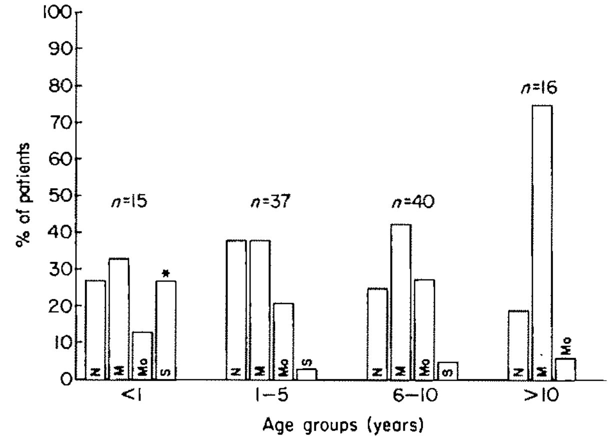

Fig. 2. Distribution of severity of hypoxaemia with age. N, none; M, mild (<95%); Mo, moderate (<90%); S, severe (<80%).

* A significant percentage of children less than one year of age had a severe decrease in oxygen saturation compared to the other groups ($p < 0.01$).

Results

The 108 children had a mean age of 5.9 years (range 10 days–14 years); 89 were ASA 1; 15 ASA 2; three ASA 3; and one ASA 4. Mean Sao_2 while breathing air before induction of anaesthesia was 96.9% (range 92–100). Figure 1 shows the distribution of decreases in Sao_2 during induction; Sao_2 decreased to less than 90% in 29 patients and less than 80% in seven patients. The lowest recorded saturation was 32% in a fit 2-year-old child during a routine nasotracheal intubation. The mean duration of decreased saturation below baseline was 47 seconds (range 0–4 minutes).

There was no correlation between ASA score and Sao_2 decrease. Figure 2 shows the relationship between hypoxaemia and age; the correlation coefficient for the whole group showed that children under one year of age were more likely to become hypoxaemic ($Sao_2 < 90\%$) than older children ($p < 0.001\%$). The effect of pre-induction condition is shown in Figure 3. Children who were anxious or crying before induction (groups 3 and 4) had a much higher incidence of hypoxaemia than children who were extremely drowsy or awake and cooperative ($p < 0.001$).

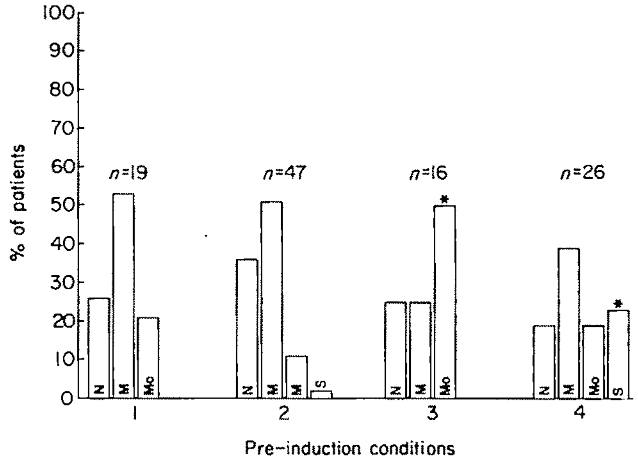

Fig. 3. Incidence of hypoxaemia in relation to pre-induction condition (see Table 1). N, none; M, mild (< 90%); Mo, moderate (< 90%) S, severe (< 80%).

* A highly significant percentage of children in groups 3 and 4 had moderate and severe hypoxaemia compared to groups 1 and 2 ($p < 0.001$).

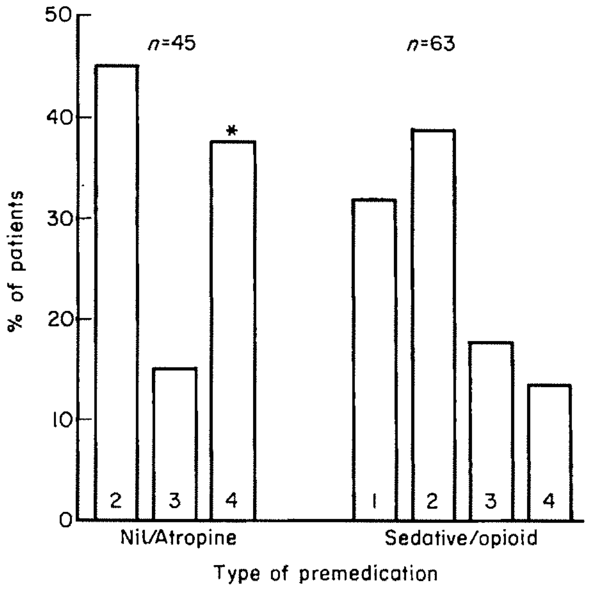

Fig. 4. Effect of premedication on pre-induction condition (see Table 1).

* A highly significant percentage of children who had no premedication or atropine alone were screaming and uncomfortable compared to those who had a sedative premedication ($p < 0.001$).

Children received one of four types of premedication: no premedication or atropine ($n = 45$); trimeprazine ± atropine ($n = 18$); diazepam ± droperidol ($n = 26$); and trimeprazine + morphine or pethidine + atropine ($n = 19$). There were no significant differences in the numbers of anxious or crying children (groups 3 and 4) among those who received one of the sedative premedications. However, children who received no premedication or atropine alone were more likely to be anxious or to cry than children given a sedative premedication ($p < 0.001$; Fig. 4). The effect of the premedication on Sao_2 (Fig. 5) showed that children who had no premedication or atropine alone were more likely to become hypoxaemic ($Sao_2 < 90\%$) than children who received a sedative premedication ($p < 0.01$).

Thiopentone was used in 81 intravenous inductions; the other agents were propofol (10) and ketamine (1). Muscle relaxation was achieved with suxamethonium (21) or

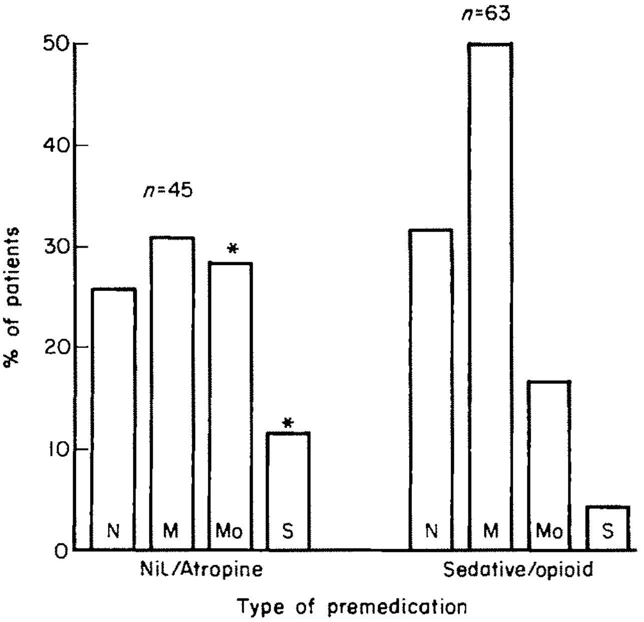

Fig. 5. Incidence of hypoxaemia with type of premedication. N, none; M, mild (<95%); Mo, moderate (<90%); S, severe (<80%).

* A significant percentage of children who had no premedication or atropine alone had $SaO_2 < 90\%$ and $< 80\%$ compared to those who had sedative premedication ($p < 0.01$).

Table 3. Incidence of hypoxaemia with type of induction.

Type of induction	*n*	Mean (SEM) lowest SaO_2	Range	Percentage of children with $SaO_2 < 90\%$
Inhalational	14	95.0 (0.6)*	91–98	0*
Intravenous/mask	37	91.4 (1.1)	63–98	27
Intravenous/oral	43	90.0 (1.4)	58–99	32
Intravenous/air	5	88.6 (3.3)	76–94	40
Awake	2	88.5 (2.5)	86–91	(50)
Intravenous/nasal	7	83.7 (8.9)	32–98	28

* $p < 0.01$ compared with intravenous groups.

vecuronium (27). Inhalational induction was achieved with nitrous oxide/oxygen/halothane (13) or nitrous oxide/oxygen/isoflurane (1). Two children were intubated awake. Mean saturation categorised by method of induction is shown in Table 3. Large decreases in SaO_2 occurred in all the intravenous induction groups; SaO_2 decreased to less than 90% in approximately 30% of children in each group. In contrast, children in the inhalational induction group had a significantly higher mean SaO_2 (95%; $p < 0.01$) and none desaturated below 90%.

Factors associated with significant SaO_2 decreases are shown in Table 4.

Table 4. Factors associated with significant hypoxaemia.

	Arterial oxygen saturation		
	80–90%	<80%	Type of induction
Respiratory depression	7	–	Intravenous/mask
Delay during intubation	2	4	Oral and nasal intubation
Delay before manual ventilation	5	–	Oral and nasal intubation
Breath-holding/coughing/laryngospasm	3	–	Intravenous/mask
Wrong tracheal tube/laryngoscopy failure	2	1	Oral and nasal intubation
Airway obstruction	1	1	Intravenous/mask
Intravenous → air	1	1	Intravenous
Difficult awake intubation	1	–	Awake
Total	22	7	

Discussion

We were surprised and alarmed at the degree of hypoxaemia found in the study as the majority of patients were fit children who presented for routine anaesthesia in a specialist children's hospital.

General anaesthesia is known to alter arterial oxygenation. Reduction in functional residual capacity (FRC), closure of small airways and associated ventilation–perfusion imbalance are among the causes in adults.[1] Children may be subject to more rapid and severe decreases in SaO_2. They have a relatively lower FRC (particularly children under one year of age) and the reduction may be exaggerated under general anaesthesia.[5] Children also have a higher basal metabolic rate, which results in increased oxygen requirements. From birth to the age of 4 months, fetal haemoglobin is present; because of its high affinity for oxygen any decrease in SaO_2 in this age group reflects a more serious decrease in arterial oxygen tension.

Induction of anaesthesia invariably results in interruption of normal alveolar ventilation and thus interference with oxygen delivery. Inhalational induction may have less effect on ventilation and in this study, any coughing or breath-holding that occurred had minimal effects on SaO_2. In contrast, approximately 30% of children who received intravenous induction had decreases in SaO_2 to less than 90% either because of respiratory depression (intravenous/mask) or because of apnoea secondary to muscle relaxants during intubation (intravenous/oral). Moderate hypoxaemia (SaO_2 80–90%) occurred with similar frequency in children who breathed through a mask and those in whom the trachea was intubated; respiratory depression was the most common cause in the former group, and delay during intubation in the latter group. Five children experienced desaturation to less than 90% because of a short delay between intravenous induction and manual ventilation of the lungs before intubation; this reflects the speed with which SaO_2 decreases in children who are apnoeic. There was also a tendency not to undertake manual ventilation of the lungs if the wrong tracheal tube was selected or laryngoscopy failed, and this increased the delay during intubation.

All the children who became severely hypoxaemic ($SaO_2 < 80\%$) were either paralysed or had partial or complete airway obstruction. The most frequent cause was delay during intubation; this occurred mainly in babies (the exception being a 2-year-old child during nasotracheal intubation). The two cases of partial or complete airway obstruction occurred in older children (aged 7 and 8 years), and air was the maintenance gas in one of these. Recent studies of SaO_2 during outpatient dental anaesthesia showed that induction with nitrous oxide/oxygen/halothane caused a negligible decrease in SaO_2[6] but that induction with methohexitone was associated with significant desaturation.[7] The relevance of the decreases in SaO_2 in the present study has yet to be determined, particularly because of their brief duration (mean 47 seconds). During everyday activities in healthy infants up to 6 months of age, the greatest decreases in saturation (down to 83%) occur during feeding.[8] No data are available for older children during coughing, crying or breath-holding, all of which may result in marked cyanosis particularly in toddlers.

Brief periods of hypoxaemia probably have no clinical significance in fit children. However, oxygen reserves are significantly reduced during hypoxaemia and any further reduction may have major consequences.[9] Hypoxaemia during anaesthesia may also be compounded by reduction in cardiac output or any other factor which interferes further with oxygen delivery to the tissues. Detection of significant hypoxaemia remains an ongoing problem particularly during induction of anaesthesia. Bradycardia is often the first sign in children but may go undetected, and cyanosis, although theoretically detectable at 89% saturation,[10] is reliably detected during anaesthesia only when Sa_{O_2} decreases below 75%.[9] Only children with saturation <80% were obviously cyanosed in the present study, and thus the presence of moderate hypoxaemia in many children was undetected by the anaesthetist.

Children who were heavily sedated became less hypoxaemic than those who were anxious or crying during induction of anaesthesia. Evelyn and Steward[11] found that there was a direct relationship in the postoperative period between a child's oxygen consumption and activity. This, possibly together with the secondary factor of hyperventilation leading to low arterial carbon dioxide tension and reduced respiratory drive, may explain our findings. Another possibility is that the anaesthetist who has finally achieved a successful venepuncture in a screaming child is so flustered (or relieved) that a slight delay occurs before airway control is maintained. Much debate continues about the most suitable premedication for children. Sedative premedication resulted in the best pre-induction conditions and the lowest incidence of hypoxaemia on induction. Patients premedicated with trimeprazine, morphine and atropine did best, despite the fact that no child received inhalational induction in this group and a higher percentage of children underwent tracheal intubation (72% compared to 58% after trimeprazine and 44% after diazepam/droperidol). The children who had no premedication or atropine only were significantly more likely to be anxious or screaming in the anaesthetic room and to have larger decreases in saturation on induction. Exclusion of children under one year of age (all of whom had atropine) did not alter these findings.

The skill of the anaesthetist is likely to influence the incidence of hypoxaemia at induction. This was confirmed by Whitcher *et al.*[12] However even children anaesthetised by an experienced anaesthetist in their study had a 10% incidence of desaturation (>10%) in the peri-operative period. Unfortunately, we did not record the experience of the anaesthetist in this study. The role and effectiveness of pre-oxygenation has not been defined in children. The adult method of applying the mask before induction may be counterproductive if it leads to greater anxiety in the child or infant. In adults, manual ventilation with 100% oxygen after induction is effective in the prevention of hypoxaemia during tracheal intubation.[13] Our demonstration that moderate hypoxaemia occurs even before manual ventilation would suggest that manual ventilation is essential in every child before tracheal intubation.

Pulse oximetry is becoming increasingly available and our study suggests that monitoring of Sa_{O_2} during induction may be of benefit in the following groups: the ill child; children under one year of age; the potentially difficult intubation; nasal intubation; and for consultants who are teaching or supervising the new junior anaesthetist. Even for the experienced anaesthetist, a period of self-audit may result in an increased awareness of the factors that result in hypoxaemia and a reduction in their incidence.

Acknowledgments

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Hypoxaemia during recovery from anaesthesia—an audit of children after general anaesthesia for routine elective surgery

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Summary

Arterial oxygen saturation was measured by pulse oximetry in 105 children (aged 2 weeks–14 years) during recovery from general anaesthesia. Oxygen saturation was monitored continuously from the time that anaesthesia ended in the operating theatre until the children were fit to leave the recovery ward. All children breathed room air during transfer to the recovery area; 81 children continued to breathe room air in the recovery ward while the remainder received supplementary oxygen. Fifty-six children became significantly hypoxaemic (oxygen saturation < 90%) at some stage. Hypoxaemia occurred most frequently after termination of anaesthesia (immediate postoperative period) and then later in the recovery ward when the children began to wake up (post-waking period). The administration of 100% oxygen at the end of anaesthesia had no effect on the incidence of early hypoxaemia which was greatest in children whose trachea had been intubated. Late hypoxaemia was associated most commonly with crying and breath-holding and was reduced significantly by supplemental oxygen. The oxygen saturation of children on return to the ward was significantly lower than the pre-operative value ($p < 0.001$).

Key words

Anaesthesia; paediatric.
Monitoring; pulse oximetry.

Hypoxaemia is known to occur after general anaesthesia, even after minor surgical procedures.[1] The majority of fit adults are transferred to the recovery room breathing room air, but it has now become accepted practice to administer supplementary oxygen routinely in the recovery area. In contrast, healthy children frequently breathe air throughout the recovery period. Recent studies of arterial oxygen saturation using pulse oximetry have demonstrated that 28% of children desaturate below 91% during transfer to the recovery room while breathing air.[2] Significant desaturation may also be present up to 15 minutes after arrival in the recovery room.[3]

The purposes of the present study were to investigate the incidence, degree and duration of postanaesthetic hypoxaemia in children after routine elective surgery and to relate this to the use of oxygen given during the recovery period.

Patients and methods

This study included 105 children (89 ASA 1; 12 ASA 2; 4 ASA 3). Their ages ranged from 14 days–14 years (mean 6.3 years). All children were scheduled for elective surgical procedures such as tonsillectomy, squint, inguinal herniorrhaphy, dental extraction/conservation (not dental chair) and orthopaedic operations. Patients who underwent thoracic or major abdominal procedures were not studied.

Forty-five children received either no premedication or atropine alone; the remainder were premedicated with trimeprazine (35), diazepam and droperidol (11), trimeprazine morphine and atropine (10) or papaveretum and hyoscine (4). Anaesthesia was induced by inhalation (13) or the intravenous route (mainly with thiopentone). Maintenance was with nitrous oxide and oxygen with or without a volatile agent. Twenty-four patients received an opioid during anaesthesia. Forty-five anaesthetics were conducted with a mask, 16 after tracheal intubation in children who subsequently breathed spontaneously, and 44 in children who were paralysed with vecuronium and who received mechanical ventilation. Muscle relaxation was reversed with atropine and neostigmine. Extubation of the trachea was undertaken in the operating theatre. Patients were transferred to the recovery ward in the lateral position and breathed air. Twenty-four patients received oxygen after arrival in the recovery room (as requested by the anaesthetist).

Arterial oxygen saturation (Sa_{O_2}) was measured continuously from the end of anaesthesia in the operating theatre until the children were ready to leave the recovery room for the ward. All recordings were made by an independent observer (G.J.A.L.), who used a battery-powered Ohmeda Biox 3700 pulse oximeter. The oximeter has a memory facility that allows the pattern of Sa_{O_2} throughout the recovery period to be studied in detail. An arterial saturation of less than 90% was considered to be clinically significant. Anaesthetists and recovery room staff were unable to see the oximeter readings and patient management was continued on clinical grounds.

The Mann–Whitney U test was used to express the results of continuous variables and the Chi-squared test for discrete variables. A value of $p < 0.05$ was considered to be statistically significant.

Results

The mean pre-induction Sa_{O_2} while the patients breathed air was 96.9% (range 92–100); this increased to a mean value of 98.7% (range 96–100) during anaesthesia. Sa_{O_2} during the recovery period followed a triphasic pattern in the majority (87%) of children (Fig. 1). Sa_{O_2} decreased rapidly from termination of anaesthesia (immediate postoperative period). It tended to plateau (prewaking period) while the children remained asleep in the recovery area and then a further decrease occurred as the children started to wake up (post-waking period); this was followed by a final increase to the waking level. The effect of supplemental oxygen given in the recovery room increased mean Sa_{O_2} significantly in the pre- and post-waking periods ($p < 0.02$), but did not influence the final Sa_{O_2}.

The mean durations of the three time periods are shown in Table 1. Fourteen children wakened immediately after termination of anaesthesia. Their saturations followed a similar pattern to the immediate postoperative period but then increased rapidly towards the waking level. Table 2 shows the detailed values of Sa_{O_2} throughout the recovery

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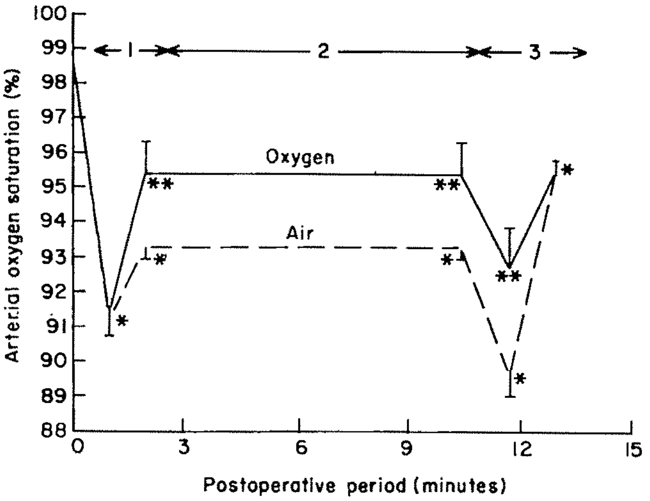

Fig. 1. Postoperative profile of Sao_2 throughout the recovery period. 1, immediate postoperative period; 2, prewaking period; 3, post-waking period. Bars represent SEM. * Sao_2 lower than pre-induction value ($p < 0.001$); ** Sao_2 higher in children who had supplemental oxygen than children who breathed air ($p < 0.02$).

period for the remaining 91 children. The highest incidences of hypoxaemia ($Sao_2 < 90\%$) occurred in the immediate postoperative period (28% of patients) and in the post-waking period (42% of patients on air and 14% on supplemental oxygen). The lowest recorded saturations were 72% in the immediate postoperative period and 69% in the post-waking period in children who breathed air, compared with 80% in those given supplemental oxygen. Detailed analysis of the immediate postoperative period showed that the difference between mean saturation was not significant for the three methods of anaesthesia (mask; tracheal intubation and spontaneous ventilation; tracheal intubation and mechanical ventilation) either at the start of, or during the first minute of, the immediate postoperative period; however children whose tracheas had been intubated were more likely to become hypoxaemic subsequently than children who breathed through a mask ($p < 0.05$; Table 3).

Sixty-eight children were given 100% oxygen by the anaesthetist before transfer to recovery; the duration of oxygen administration varied according to the normal clinical practice of the anaesthetist but was usually between 1 and 3 minutes. No significant difference was found in the incidence of hypoxaemia in the immediate postoperative period between children who received oxygen at this time and those who did not (Table 4). Hypoxaemia occurred in 56 children at some stage during recovery. The most common associated factors (Table 5) were crying and breath-holding in the post-waking period and extubation of the trachea in the immediate postoperative period. Vomiting during recovery occurred in only three children. The airway was well maintained in all of these and none desaturated below 90%. Coughing occurred frequently during recovery but was associated with significant desaturation in only one child. The mean Sao_2 at the time of discharge from the recovery room to the ward was 95.6% (range 89–100). This was significantly less than the pre-induction saturation ($p < 0.001$).

Table 1. Recovery from anaesthesia (minutes).

	Mean	Range
Immediate postoperative period	2	0.25–5
Prewaking period	8.5	1–20
Post-waking period	2.5	0.5–5

Table 3. Sao_2 after the first minute of the immediate postoperative period.

Anaesthesia	n	Sao_2 (SEM)
Mask	45	92.3 (0.9)
Intubated + IPPV	44	91.2 (0.8)*
Intubated + spontaneous ventilation	16	89.3 (2.0)*

* Children whose trachea was intubated had a significant decrease in Sao_2 from pre-induction values compared to those who breathed through a mask ($p < 0.05$).

Table 4. Effect of 100% oxygen before tracheal extubation on immediate postoperative decrease in Sao_2.

	No decrease	Decrease to 90%	85–89%	<85%
Oxygen (n = 68)	5	44	11	8
No oxygen (n = 37)	5	27	2	3

$p < 0.3$.

Table 5. Factors associated with significant hypoxaemia ($Sao_2 < 90\%$); n = 105.

Crying/breath-holding	31
Postextubation	15
Airway obstruction/snoring	5
Severe respiratory depression	4
Coughing	1
Total	56

Discussion

Our study has shown that 54% of children had an arterial oxygen saturation below 90% at some stage during recovery. The largest decreases in saturation occurred immediately after anaesthesia, and later in the recovery room

Table 2. Sao_2 during recovery from anaesthesia in children (n = 91).

	Gas	Mean (SEM)	Range	Percentage of patients with $Sao_2 < 90\%$
Sao_2 (pre-induction)	A	96.9 (0.2)	92–100	–
Sao_2 (intra-operative)	An	98.7 (0.1)	96–100	–
Immediate postoperative decrease	A or O	91.2 (0.6)*	72–98	28
Prewaking	A	93.8 (0.3)*	88–98	5
Prewaking	O	95.4 (0.8)**	86–100	5
Post-waking	A	89.7 (0.6)*	69–98	42
Post-waking	O	92.7 (1.1)**	80–99	14
Sao_2	A	95.6 (0.2)*	89–100	1

A, air; An, 33% oxygen in nitrous oxide; O, supplemental oxygen by facemask.
* Sao_2 significantly lower than pre-induction value ($p < 0.001$); ** Sao_2 significantly higher in children who breathed oxygen compared to those who breathed air ($p < 0.02$).

when the children started to awaken. The lowest recorded $S\text{ao}_2$ was 69%.

A review of aetiology and severity of postoperative hypoxaemia in adults in 1972[4] reported decreases in $P\text{ao}_2$ to 7.9 kPa in the first 30 minutes after surgery; however, measurements were restricted by the intermittent and invasive nature of blood gas measurement. Pulse oximetry provides reliable, noninvasive measurement of $S\text{ao}_2$.[5] Detailed studies of $S\text{ao}_2$ in patients who breathed air during transfer from the operating theatre to the recovery area, have shown that $S\text{ao}_2$ decreases to less than 91% in 35% of adults[6] and 28% of children.[2] These decreases occurred despite the administration of 100% oxygen for 5 and 3 minutes respectively before transfer. In the present study, only 65% of children received 100% oxygen and $S\text{ao}_2$ decreased to less than 90% in 28% of patients.

Oxygen administration for 3 minutes is practised on the assumption that it prevents diffusion hypoxia caused by nitrous oxide elimination. The clinical relevance of diffusion hypoxia is still disputed, but evidence suggests that nitrous oxide elimination may result in a decrease of $P\text{ao}_2$ to less than 8 kPa for at least 5 minutes.[7] Vijayakumer *et al.*[8] showed a reduction in the incidence of hypoxaemia when 100% oxygen rather than a 50:50 mixture of oxygen and air was administered for 3 minutes. Our study showed no difference in the incidence of hypoxaemia between patients who received 100% oxygen and those who breathed air at the end of anaesthesia.

Factors other than nitrous oxide also cause hypoxaemia at this early stage of recovery. Our study identified extubation of the trachea as a significant cause of hypoxaemia, as a result mainly of breath-holding and the associated decrease in ventilation. Other studies[2,6] have shown that anaesthetic drugs, use or avoidance of opioids, use of controlled or spontaneous ventilation, duration of anaesthesia and age had no influence on $S\text{ao}_2$ during transfer from the operating theatre, although a further study[9] found that children under one year of age have a higher incidence of hypoxaemia. Few studies have measured $S\text{ao}_2$ after arrival in recovery while breathing air. Motoyama *et al.*[3] found that 43% of children desaturated below 91% throughout transfer and recovery, but measured $S\text{ao}_2$ for only 15 minutes in the recovery room; there was a rapid increase in $S\text{ao}_2$ when the children woke up, a finding which has been confirmed in the present study.

Detailed studies of the effects of type of premedication, method of anaesthesia and type of surgery on $S\text{ao}_2$ during recovery have not been conducted, although Motoyama *et al.*[3] found no statistical difference between children who received inhalational anaesthesia alone and those who were given opioids. We compared unpremedicated children and those who had received atropine only with those who were given a sedative premedication (excluding all opioids). The mean duration of the prewaking period was higher (9.5 minutes) in children who received a sedative than those who did not (7.5 minutes; not statistically significant), but there was no difference in the incidence of hypoxaemia throughout the whole recovery period. We were unable to analyse the opioid group because many of them had no volatile agent. A study in children who underwent outpatient surgery,[10] and who had no premedication, but inhalation induction followed by maintenance with nitrous oxide, oxygen and halothane, showed that no child desaturated below 93% during recovery. The exact relevance of desaturation below 90% has yet to be determined. Healthy infants desaturate to 83% while feeding and some authors consider severe desaturation to be less than 65%.[2] Yelderman[5] reduced the inspired oxygen concentration of five healthy adults until the arterial saturation was 70% while awake, with no untoward effects. The duration of hypoxaemia is obviously of relevance. The major periods of desaturation in our study were of short duration (less than 5 minutes).

In conclusion, we have demonstrated the pattern of $S\text{ao}_2$ throughout the whole of the recovery period. We consider that the maintenance of a clear airway and satisfactory ventilation are of primary importance. Despite careful clinical care, periods of desaturation to less than 90% occur in a significant proportion of children. $S\text{ao}_2$ increases rapidly when the children are awake and although their final saturation is significantly lower than pre-induction saturation, this probably has no clinical relevance after minor surgery. We have been unable to show any significant reduction in hypoxaemia in children who received 100% oxygen before transfer to the recovery room, but the incidence of hypoxaemia was significantly reduced by the use of oxygen during subsequent recovery.

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HIV infection, AIDS and ICU in Central Africa

The article by Deam, Kimberley and Anderson (*Anaesthesia* **43:** 150–1) raised the controversial issue of HIV antibody screening of patients admitted to ICUs. Recently, we screened 396 admissions to the ICU in the University Teaching Hospital, Lusaka, Zambia. None of these patients were known to be HIV seropositive on admission. Eighty-one (20.5%) patients were HIV seropositive on testing, but the hospital outcome was similar in both seropositive and seronegative patients.[1] The only subgroup of seropositive patients who had a worse outcome were those who were subsequently found to have HIV-related pneumonias.

A distinction needs to be made between HIV seropositivity and clinical AIDS. In our unit, patients who are critically ill but whose illness is not directly related to their HIV infection do as well during their hospital stay as those who are seronegative. In contrast, the majority of patients who are critically ill with HIV-related pneumonias, tuberculosis or other HIV-related pathologies such as Kaposi's sarcoma die in hospital. Screening alone should not determine admission policies. AIDS is fundamentally a clinical diagnosis and it is the clinical findings that should influence the decision whether to admit or not. There is little benefit in our experience to be gained from the provision of intensive care services to those with AIDS but neither should someone be denied those services on the basis of an HIV result alone.

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I.H. Wilson

Reference

1. Watters DAK, Sinclair JR, Luo N, Verma R. HIV seroprevalence in critically ill patients in Zambia. *AIDS* 1988; **2:** 142–3.

A reply

The letter from Watters and Wilson reports some interesting observations. The screening of 396 admissions to ITU allows them to make a realistic assessment of the prevalence of positive HIV status amongst their ITU admissions. This information is not available in the UK because of the restrictions on testing. Instead we have an awareness of an increasing number of HIV positive patients passing through our ITU. Nevertheless, figures such as those reported of

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20% are certainly considerably higher than in our own community currently. We are aware that the epidemiology of the disease may vary between countries, but these figures are of interest in the evaluation of potential future developments, especially in the absence of meaningful statistics of our own.

It is already becoming apparent that the majority of HIV-positive patients admitted through ITU do not have HIV-related illness. This is hardly surprising as the number of seropositive individuals in the community is far greater than the number with AIDS and it is only reasonable to expect increasing seropositive non-AIDS-related ITU admissions. It is also a reflection on the changing clinical approach with less ITU referral for AIDS-related problems. However, there is increased 'ward' procedural work done by ITU staff, for example, placement of central lines.

The observation that the outcome of HIV-positive patients appears to be the same as the negative patients is of particular interest. This information is not only unavailable in this country but is not likely to become available in the foreseeable future if we are not aware of which patients are negative and positive. Furthermore the question of whether the seropositive group are predisposed to specific problems when critically ill is unlikely to be answered.

We agree with the authors that HIV screening should play no part in the decision to admit to ITU. However testing is helpful since clearly HIV-positive status may contribute diagnostically in the acute setting characteristic of many ITU admissions. However, when the cause of admission is AIDS related, other factors, such as the probable poor outcome, must be considered. Equally the rapid evolution of AIDS therapeutics demands continual reassessment of the role of ITU management in AIDS.

In conclusion it is obvious that we would gain from further information from the areas where there is a high prevalence of seropositivity and where statistics are available. The particular areas to be addressed include whether any predisposition exists for problems other than AIDS or ARC during critical illness (although this letter suggests that this is not the case.) The real relevance of this data will remain conjectural while testing is not an accepted part of ITU practice.

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A.P.S. KIMBERLEY
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M. ANDERSON
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Continuous lumbar plexus block after arthroplasty

In a recent investigation[1] the analgesic effect of a continuous block of the lumbar plexus with bupivacaine was compared with sodium chloride in 20 young patients with postoperative pain after knee-joint surgery (reconstruction of cruciate ligaments, operations for malposition of the patella). The patients who were treated with bupivacaine had significantly lower pain scores and a significantly lower demand for morphine. We report our preliminary results with continuous block of the lumbar plexus with bupivacaine after knee arthroplasty.

Twelve patients participated in the investigation, and all gave their informed consent in accordance to the Helsinki II declaration, and the investigation was approved by the regional ethics committee. Anaesthesia was induced with thiopentone and pethidine intravenously and maintained with enflurane 0.8–1.5%, nitrous oxide and pethidine when needed. Tracheal intubation and controlled ventilation of the lungs was used. A catheter (Portex, epidural, 16-G) was placed in the fascial sheath of the femoral nerve and advanced 5–20 cm cranially before surgery and while the patients were awake.

The patients were randomized into two groups to be treated with the same volume of either bupivacaine or isotonic sodium chloride by way of the catheter as described earlier.[1] Infusions were started before surgery and continued for 16 hours postoperatively. Morphine was administered postoperatively in addition when needed. The intensity of pain was recorded on a visual analogue scale 2, 4, 6, 8, 12 and 16 hours after operation. Table 1 summarises the data.

No significant differences (Mann–Whitney *U* test, $p > 0.05$) were found between the bupivacaine-treated and the NaCl-treated patients in consumption of intra-operative pethidine (median 1.5, as against 1.6, mg/kg), postoperative morphine (median 0.29, versus 0.41 mg/kg/16) or pain intensity (median 11, as against 48, mm) although both the consumption of postoperative morphine and the pain scores were reduced in the bupivacaine group. However, all the patients in this group needed morphine, 13–26 mg/16 hour.

Table 1. Demographic data of patients with median values and ranges. No significant differences ($p > 0.05$) were found (Mann–Whitney *U* test).

	Bupivacaine	NaCl
Males/females	1/5	1/5
Age, years	72 (63–87)	70 (60–78)
Height, cm	161 (158–170)	163 (156–174)
Weight, kg	70 (60–78)	77 (59–87)
Duration of surgery, minutes	120 (90–195)	113 (105–135)
Peroperative pethidine, mg/kg	1.5 (1–1.9)	1.6 (1.3–2.3)

The present investigation differs from our previous study[1] in that surgery involved more structures innervated by the sciatic nerve (tibia). Furthermore, the patients were older and some found it difficult to use the visual analogue scale, which makes interpretation of the results more difficult.

We conclude, in spite of a considerable risk of a type II error, that although a certain morphine-sparing effect of continuous blockade of the lumbar plexus can be expected, the method does not seem to be advantageous as pain treatment after knee arthroplasty.

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Reference

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Sedation with isoflurane

We were interested to read the anecdotal report from Drs Beechey and colleagues. (*Anaesthesia* 1988; **43:** 419–20) but we question the wisdom of routine use of such an agent before the results of carefully conducted trials have been reported.

We reported, after a pilot study conducted in 1986 in the Bristol Royal Infirmary, that isoflurane is a useful agent for the sedation of ventilated patients in the intensive care unit.[1] Preliminary findings of a definitive controlled trial that compared isoflurane with midazolam, for the sedation of ventilated patients with a range of severity of illness, show that the quality of sedation and the speed of recovery is significantly better with isoflurane than with midazolam.[2] Provided that patients are not hypovolaemic, the use of subanaesthetic concentrations of isoflurane to sedate ventilated patients does not have any deleterious effects on haemodynamic stability. Isoflurane sedation for up to 24 hours had no adverse effects on hepatic, renal and adrenocortical function, haematological and biochemical variables in our patients.

We agree that isoflurane shows considerable promise in this application, but we believe that it is premature to advocate routine use of isoflurane before the results of carefully conducted trials have been fully reported.

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K.L. KONG
S.M. WILLATTS
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Seizure duration and propofol

Dr Dwyer and colleagues (*Anaesthesia* 1988; **43:** 459–62) report that propofol reduces seizure duration in electroconvulsive therapy (ECT), as compared to methohexitone, and state that this may result in the need for more ECT treatments to achieve the same therapeutic effect. They quote a paper by Maletzky,[1] which is very dated in terms of ECT research. Maletzky used multiple monitored ECT, (3–4 shocks at each treatment) a practice not commonly used in Britain now. His subject group was diverse, and included patients with diagnoses of schizophrenia, compulsive neurosis, and chronic pain.

Two subsequent more methodologically rigorous trials[2,3] have shown no relationship between any aspect of seizure duration and clinical effect. However, both arbitrarily chose 25 seconds of seizure duration as the lower limit for an 'adequate' seizure.

Dwyer's paper confirms two previous reports[4,5] that propofol decreases seizure duration in ECT, though it is unknown if this is undesirable. Indeed, propofol may even be beneficial in ECT, since there is some evidence that it is release of endogenous inhibitory neurotransmitters which terminate the seizure, and these substances subsequently exert the antidepressant effect by way of interactions with monoamines.

Anaesthetists should not be dissuaded from using propofol in ECT, on the grounds that it may impair efficacy until a study is performed that compares outcome in depression between propofol and methohexitone groups.

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J. SEYMOUR

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A reply

We are glad to state that we share Dr Seymour's high opinion of propofol. The work of Maletzky may be criticised, but neither of the other studies which he quotes set out primarily to identify a relationship between seizure duration and therapeutic benefit. Indeed, Weiner *et al.* attempted to control seizure duration to between 25–60 seconds, which must limit the possibility of finding any link. Sackheim and colleagues also do not, in fact, disagree with Maletzky's conclusions, although they offer their own alternative explanation, and report better therapeutic outcome in subjects with lower seizure threshold. There is other more recent work in Britain[1] which shows that, using a constant current device, there is a positive correlation between seizure duration and therapeutic outcome.

We therefore consider that this relationship remains at least a distinct possibility, and thus we have no alternative but to draw attention to this in our paper. Whether there is in fact any difference in therapeutic outcome after propofol as compared to methohexitone for ECT is a question which, as Dr Seymour suggests, must await answer until a study is carried out. We did not, indeed could not in view of the crossover design, look at this aspect in our study.

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R. DWYER
W. MCCAUGHEY
R.J. MCCLELLAND

Reference

1. MCCLELLAND RJ, HEADLEY M, LAWLESS V. EEG monitoring in electroconvulsive therapy. *Journal of Electroencephalography and Clinical Neurophysiology* 1987; **70:** 70.

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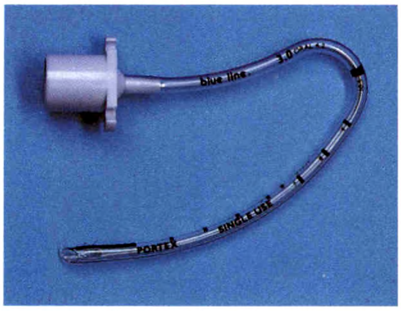

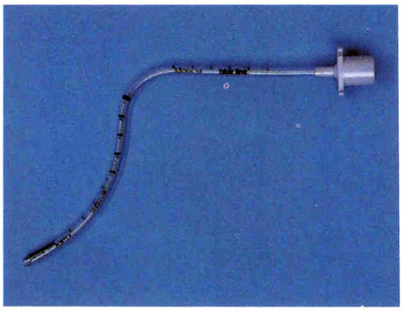

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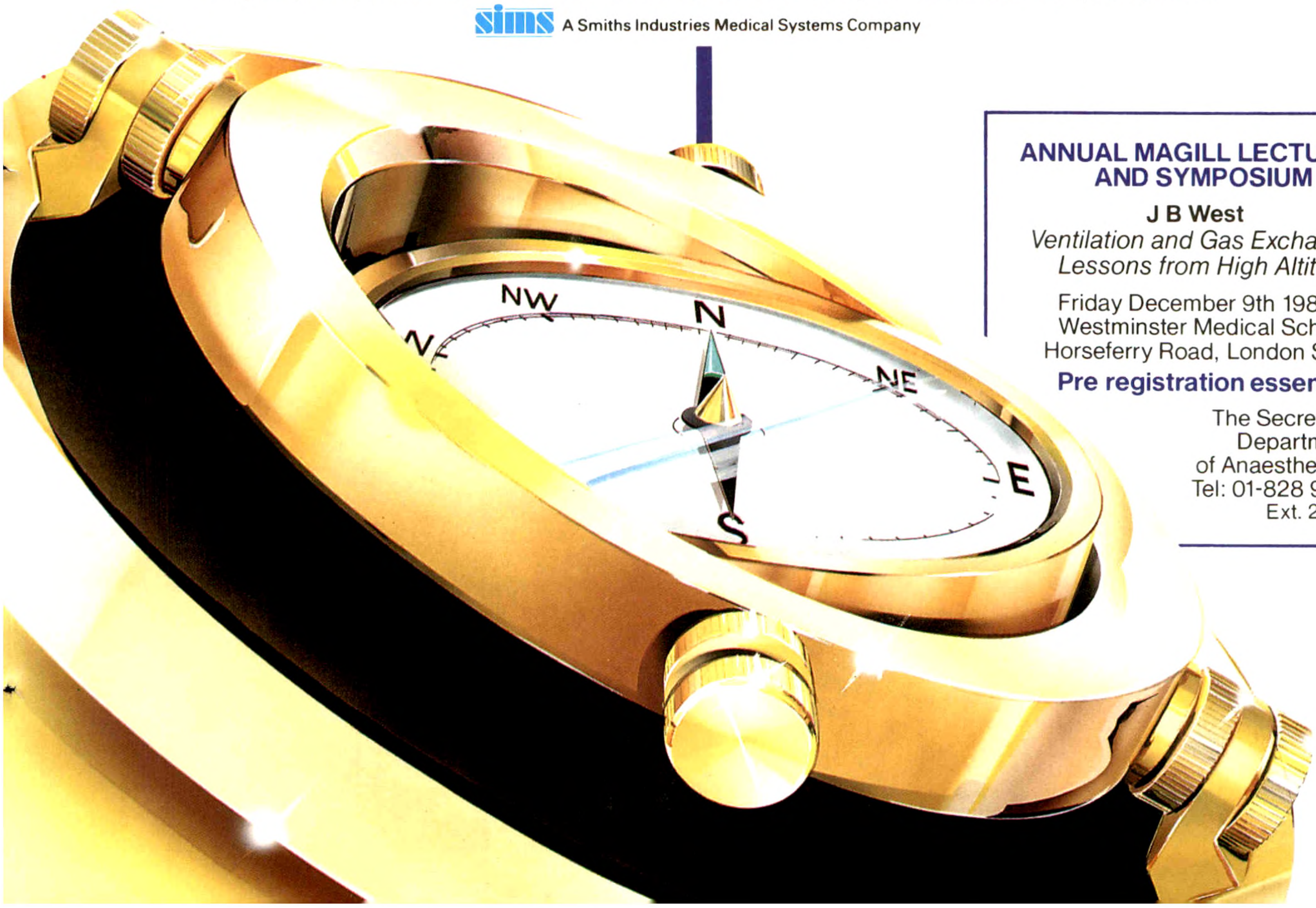

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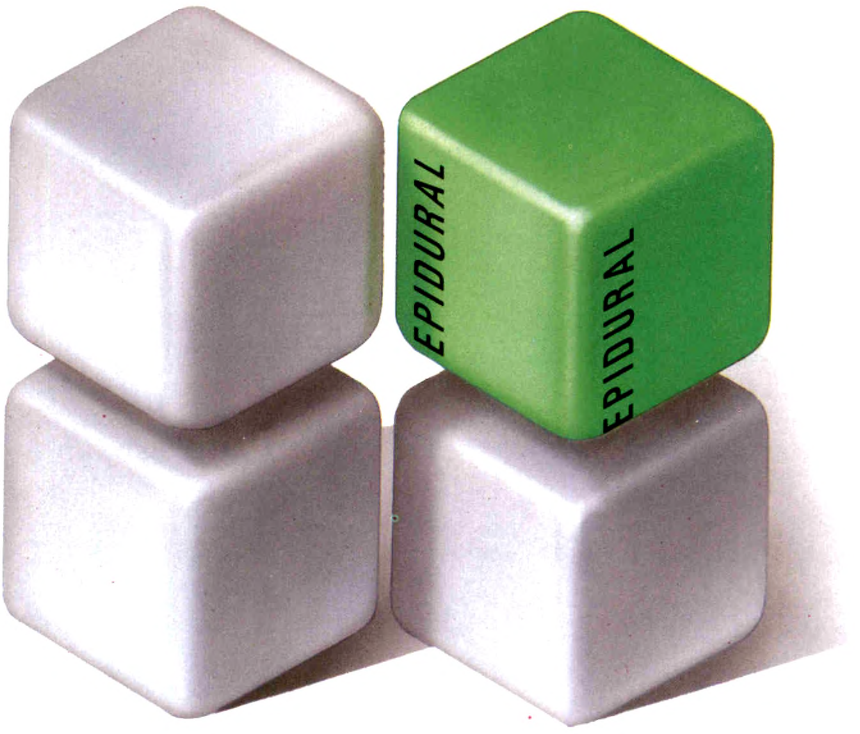

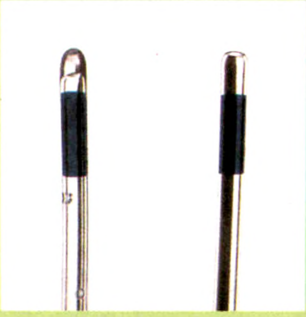

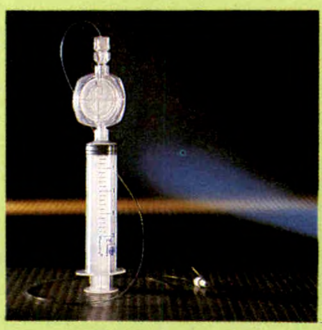

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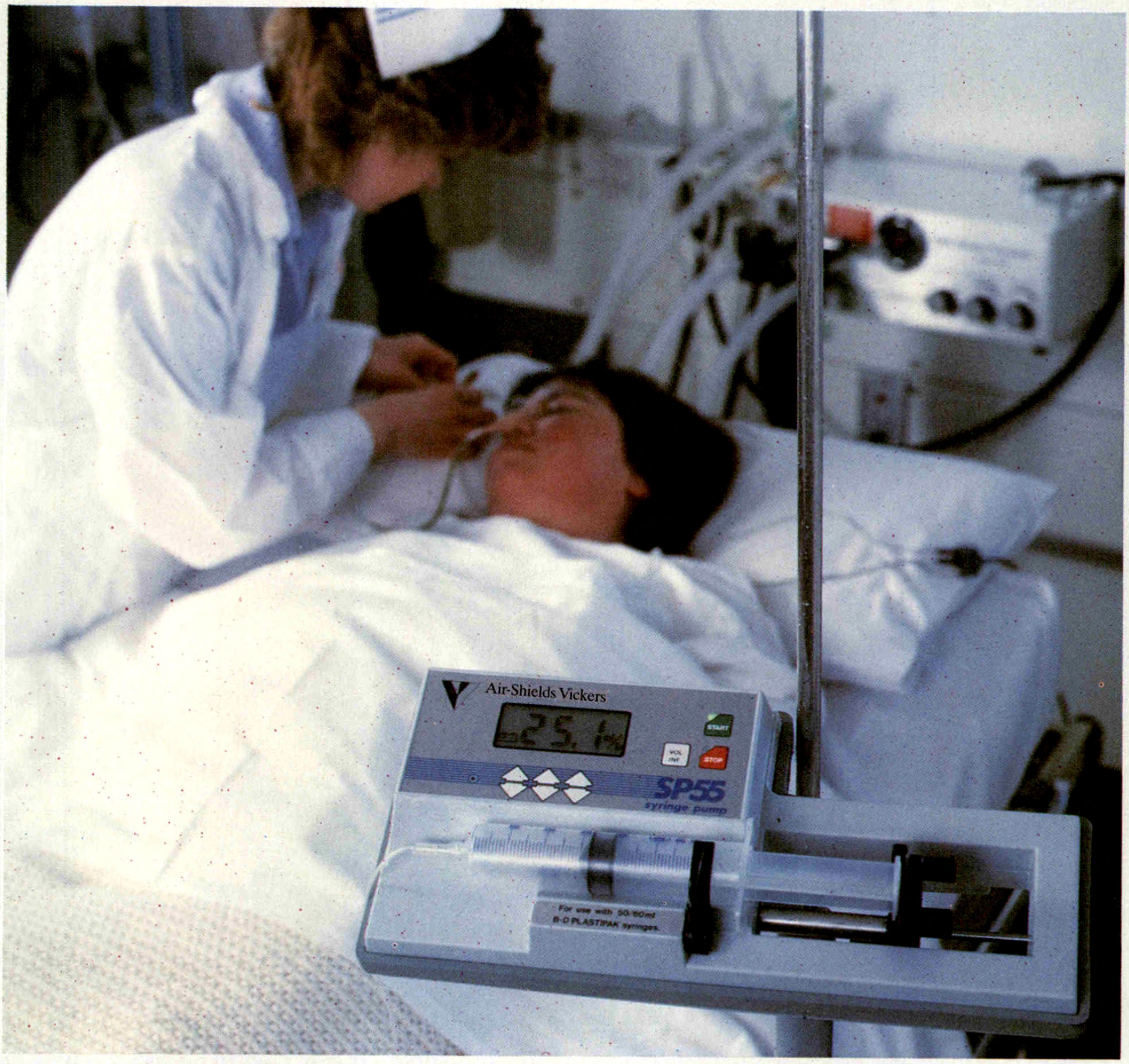

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Trichloroethylene

The report on clinical use of trichloroethylene in the final issue of the Forum for 1987[1] delighted me. Trichloroethylene is a marvellous analgesic (as demonstrated by the authors) and low in cost. One is forced to assume the reason commercial purveyors abandoned promotion of the drug was the limited profit possible secondary to low price and the low concentrations necessary for analgesia.[2,3]

Here is some history for your younger readers. Reference 7 of the Rice and Reynolds report should perhaps be changed to either:

> Jackson DE. A study of analgesia and anesthesia, with special reference to such substances as trichlorethylene and vinesthene (divinyl ether), together with apparatus for their administration. *Anesthesia and Analgesia* 1934; **13**(5): 198–203; or Striker C, Golblatt BS, Warm IS, Jackson DE. Clinical experiences with the use of trichlorethylene in the production of over 300 analgesics and anesthesias. *Anesthesia and Analgesia* 1935; **14:** 68–71.

The Hewer article cited by the authors (their reference 7) was 'With a prefatory note by Charles F. Hadfield, MBE, MD, DA, . . . Honorary Secretary of the Joint Anaesthetics Committee of the Medical Research Council . . .' Dr Hadfield recounted receipt of a letter from Mr C. Chalmers of Muswell Hill concerning trichlorethylene (*sic*) at a time when a nonflammable anaesthetic was being sought to replace chloroform for casualties. Dr Hewer confirmed trichloroethylene's clinical utility and introduced the drug to general use.

Stephen and Slater introduced the drug into Canadian and American use after the war.[4] Prior, of the Christian Medical College in India, noted the economy and safety of trichlorethylene (*sic*) in air with muscle relaxants.[5] Over a decade ago Crawford advocated 'A return to trichloroethylene for obstetric anaestheisa'.[6] A past President of the Association, Michael Rosen, reported on the utility of trichloroethylene in air in obstetric anaesthesia.[7] (Methoxyflurane in air was considered superior to trichloroethylene, but fear of fluoride poisoning has terminated the popularity of methoxyflurane.)

Other bits of trichloroethylene lore include a comment about the author of the only text on the drug.[8] The author, Gordon Ostlere, DA, is better known to the nonmedical world as Richard Gordon, author of the 'Doctor in the House', books. Dennis E. Jackson, the discoverer of trichloroethylene as a general anaesthetic, was a 1913 graduate of Rush Medical College. In 1915, Jackson introduced the closed carbon dioxide absorption system of general anesthesia.[9] Jackson wished to reduce waste of nitrous oxide and thereby reduce the cost of a general anaesthetic (50c) for the poor patients treated in the Rush surgical clinics. Rush Medical College graduates introduced ethylene as a general anaesthetic (A.B. Luckhardt, class of 1912) in 1923 and demand-flow anaesthesia circuits (E.I. McKesson, class of 1906).

A clinical comment concerning use of trichloroethylene may be of value. A third of a century ago it was common practice to administer small doses of pethidine intravenously, as necessary, to prevent tachypnea (Pembleton made the same recommendation 14 years ago).[10] Gently assisted ventilation was used to assure a 'soft' brain during neurosurgical procedures. With trichloroethylene, one knew immediately when the retractor was in the wrong place, especially with posterior fossa tumours. In this country availability of the drug has been limited since it is said to cause tumours in mice. You are fortunate to have the drug in the UK. It is to be hoped that Rice and Reynolds report will encourage employment of this useful low-cost analgesic-anaesthetic.

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Illinois 60612,
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J.B. Stetson

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Insulation of needles

Please let it not be writ 'That there is now clear evidence that uninsulated needles should not be used with nerve stimulators' (*Anaesthesia* 1988; **43:** 509), especially when referenced with our and Bashein's papers.[1,2] These papers simply showed that for uninsulated needles the point of maximum current density was 0.5 cm from the needle tip, they made no recommendations about the use of such devices and I know of no other data to support the above assertion.

Uninsulated needles are extremely cheap, available in every anaesthetic room in the country and for most blocks work extremely well. If Dr McNicol has some data on the incidence of neuralgia after their use perhaps he would share it with us. If not we would surely do better to try to prevent neural damage by encouraging the use of the nerve stimulator rather than by searching for parasthesiae. Most hospitals have a nerve stimulator; few have insulated needles. The use of standard needles enables any interested party to use the technique to the benefit of patients.

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C.E. Pither

References

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Failure of the expiratory valve on a Bain system

We wish to report the failure of a Mediplast Valve (Coax 1) on a Bain anaesthetic system during the induction of anaesthesia, such that it was impossible to close the system and inflate the patient's lungs.

The Mediplast Coax 1 Valve is made of lightweight materials and is autoclavable. It is so constructed that it is possible to dismantle the valve to replace the internal parts when required. The valve is designed to automatically 'blow off' at a predetermined pressure normally 6.0 kPa. This pressure is set using the tension locking screw (Fig. 1, A). The tension locking screw is immobilised with a fixative once the valve is assembled and this pressure checked.

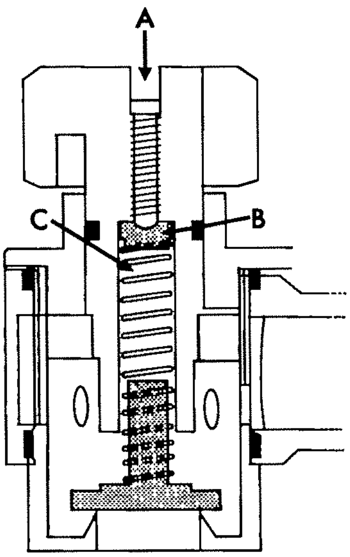

Fig. 1. The Mediplast (Coax 1) valve. A, tension control screw; B, plastic insert; C, pressure limiting spring.

It was discovered, when the offending valve was examined that a fault had occurred during reassembly. The plastic inset (Fig. 1, C) above the pressure controlling spring (Fig. 1, B) had accidentally been omitted. Furthermore, the tension control screw had not been immobilised with Locktite 222 as recommended by the manufacturer.

These errors allowed the valve to appear to function normally at first. The opening and closing of the valve during routine use with the spring and tension controlling screw in contact caused a turning force. This led to the progressive loosening of the screw so that the screw could turn as the valve was operated. Eventually a situation occurred when all tension in the spring was lost and the valve could not be closed.

This incident has been reported to the manufacturer and the Common Services Agency under the hazard notification procedure.

Royal Hospital for Sick Children,
Yorkhill,
Glasgow G3 8SJ

D.C. Miller
J.W. Collins
L. Wallace

A reply

All valves at present in use have been checked to ensure correct assembly. A letter has also been sent to all users to discourage the disassembly of Coax 1 valves.

Any valves which require service or repair should be sent back to Mediplast Ltd., where the appropriate repair or service will be carried out.

Mediplast Ltd,
15 Fleming Close,
Wellingborough,
Northants NN8 3UF

G. Young

Accidental extubation and low air loss mattresses

Accidental tracheal extubation of patients is a well known hazard in intensive care. This is a report of an incident with unusual features.

An elderly female who was recovering from septicaemia secondary to osteomyelitis was receiving controlled ventilation of her lungs through a nasotracheal tube. She had severe rheumatoid arthritis and loss of weight so she was nursed on a low airloss mattress (Medicus Products Ltd., Whareham, Dorset) to protect her pressure areas.

A disconnexion in the air supply caused the segment of mattress which supported the thorax to collapse. The patient moved a significant distance downwards and, since the ventilator tubing was attached to a rigid support, the tracheal tube was withdrawn from the larynx. The patient was fortunately able to start breathing spontaneously and did not come to any harm. She did not in fact require reintubation so, although the extubation was unplanned, it was not untimely.

This type of malfunction is apparently not uncommon, according to the nurses, so I recommend that, if a low air-loss mattress is used for a patient at risk of disconnexion then fixed supports should be abandoned in favour of fixation of the tubing to the pillow or sheet, which will move with the patient's head should a malfunction occur.

University College Hospital,
London WC1E 6AV

P.Q. Smeele

Sudden ventricular dysrhythmias after unintentional mediastinal washout with tetracycline containing solution

A 33-year-old, previously fit, woman who weighed 45 kg was anaesthetised for total oesophagectomy for oesophageal stricture after an earlier ingestion of bleach.

Anaesthesia was induced with etomidate, muscle relaxation achieved with suxamethonium followed by alcuronium, and anaesthesia was maintained with 65% N_2O and 0.5–1.5% enflurane in O_2. Incremental doses of fentanyl were given intravenously and totalled 500 μg. A laparotomy was performed and both the stomach and oesophagus were mobilised and brought through the diaphragmatic hiatus to the neck, a fundo-oesophageal anastomosis was successfully performed and a thoracotomy was not required.

Towards the end of an uneventful anaesthetic and just before closure of the peritoneum, 2 litres of normal saline, at room temperature, containing 1 G tetracycline were poured into the peritoneal cavity, some of which found its way unintentionally into the mediastinum. The washout solution was sucked out within 2 minutes.

The patient developed frequent episodes of ventricular tachycardia (up to 10–12 ectopic beats/run) during the next

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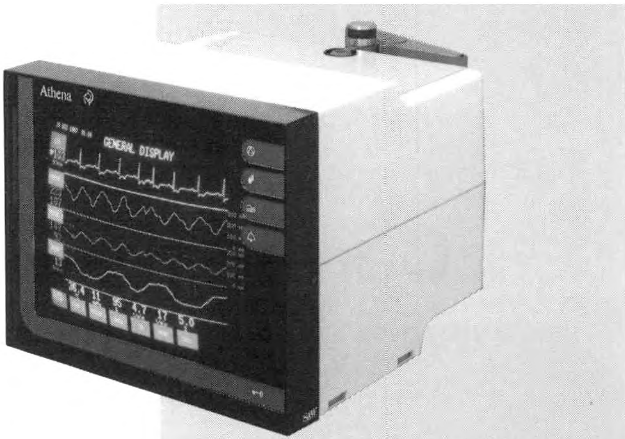

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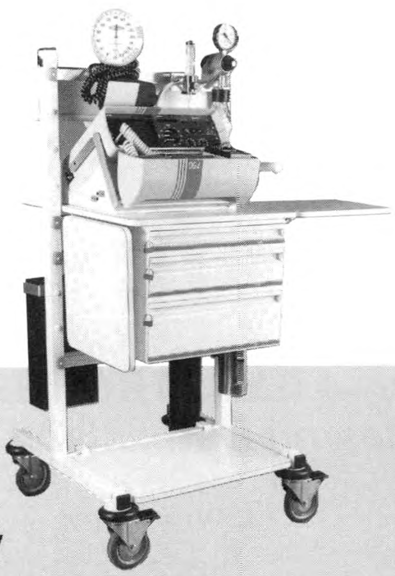

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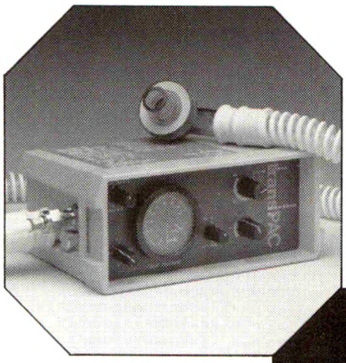

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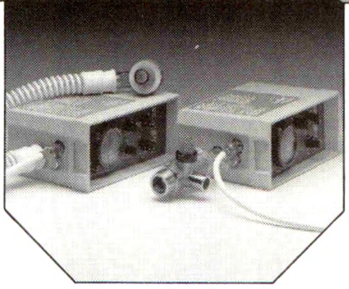

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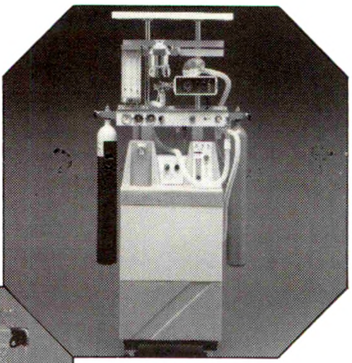

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30 seconds and this persisted for about 20 minutes in spite of immediate withdrawal of enflurane and administration of lignocaine in bolus doses up to 120 mg. Sinus rhythm was maintained between these ventricular runs. The blood pressure, recorded from an arterial line and O_2 saturation, recorded from a pulse oximeter were within normal limits and end-tidal CO_2 was 4.5 kPa. The blood gases, acid/base and blood biochemistry were within normal limits except K^+ was relatively low (3.4 mmol/litre) compared to the preoperative value of 4.2 mmol/litre.

Gradually over the next 20 minutes, occasional ventricular ectopics (VEs) were still present (up to 3–5 VEs/minute) and neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrronium 0.6 mg. She was awakened promptly, her trachea extubated, observed in the ITU and made an uneventful postoperative recovery.

Peritoneal lavage is a standard technique commonly performed in the course of abdominal surgery.[1,2] We suggest the possible causes of these ventricular dysrhythmias in our patient may include: first and the most obvious is mechanical cold stimulation of the heart at the time of relative hypokalaemia which caused these dysrhythmias to persist for longer than expected. Secondly, local damage or irritation of the autonomic nerves near the pericardium caused by surgical dissection and the high power suction may have been additional factors in the sudden development of these dysrhythmias and made them refractory to treatment.

There appear to be no published reports of cardiac dysrhythmias following operative lavage of the mediastinum and we are interested to hear of any similar problem experienced by other anaesthetists or surgeons.

Royal Hallamshire Hospital, M.S. YOUSSEF
Sheffield S10 2RX

References

1. STEWART DJ, MATHESON NA. Peritoneal lavage in appendicular peritonitis. *British Journal of Surgery* 1978; **65:** 54–6.
2. MATHESON N.A. Perforated appendix—a plea for lavage. *British Journal of Surgery* 1979; **66:** 293–4.

The drawover Boyle's machine—a safe alternative

Sinclair and Wilson (*Anaesthesia* 1988; **43:** 405–8) have described an ingenious adaptation of the Boyle's machine, but the risks of misconnexion and barotrauma are causes for concern. The authors do recognise these hazards, but do not seem to have considered the alternative solution which avoids such problems cheaply and with less modification.

It is a simple matter to remove the Oxford Miniature Vaporizer (OMV) from the backbar, substitute a suitable length of piping, and attach the OMV directly to the drawover breathing system. A T-piece and reservoir could be fitted to the other port and oxygen supplied, if necessary, from the common gas outlet or from a spare cylinder. The Triservice adapted OMV[1] is free-standing and might be a more suitable alternative. This manoeuvre is only slightly more complex than the system change described by Sinclair and Wilson and must be considerably cheaper than the modifications which they suggest. There is no risk of barotrauma since the system is open to the atmosphere. It is also unnecessary to disable the pressure-relief valve which can still protect the Boyle's machine as intended by the manufacturers. In addition, if the actual Laerdal 23-mm taper system is used, (the system in Fig. 5 is not Laerdal as claimed) then there is no risk of misconnexion.

The OMV does not vaporize efficiently at one litre/minute continuous oxygen flow, if at all.[2] The drawover circuitry is therefore diluted by a low concentration of halothane when the non-rebreathing valve is closed and the patient receives less than the indicated concentration when it is open. This might help to explain the lightening of anaesthesia experienced by Sinclair and Wilson, although cooling of the vaporizer exacerbates this effect. If the vaporizer is used as above, the problem does not occur. It is a pity that the authors did not measure the FiO_2 in the drawover mode. One would not feel entirely confident about the adequacy of oxygenation with one litre/minute and the arrangements suggested. Oxygen might spill over at the Heidbrink valve at the high flows necessary for preoxygenation and I would expect a T-piece system to be more economic.

It is most unfortunate that purpose-built drawover apparatus is not more widely used in the third world and that previous recommendations to this effect are ignored. If developing countries were encouraged more forcibly in this direction by those in a position to do so, then there would be no requirement for the not so happy happy-medium suggested, future morbidity might be avoided and money saved.

Glasgow Royal Infirmary, S.Q.M. TIGHE
Glasgow

Reference

1. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36:** 1094–108.
2. SCHAEFER HG, FARMAN JV. Anaesthetic vapour concentrations in the E.M.O. system. *Anaesthesia* 1984; **39:** 171–80.

Drs Sinclair and Wilson's ingenious modification of the Boyle International machine for drawover anaesthesia (*Anaesthesia* 1988; **43:** 405–8) was interesting and this is a comment on the second of the potential hazards which they discuss.

The need for a pressure-relief valve, such as an open Heidbrink valve, to prevent jamming of a non-rebreathing valve in the inspiratory phase when using a continuous flow of gases has been desirable since the days of the Ruben valve. However, some more modern non-rebreathing valves have been designed to allow a forward flow of gas through them without jamming.

I have tested a number of these using a Blease respirable air pump. The patient port on each valve was blocked and the maximum forward flow which the valve allowed without a build-up of pressure (i.e. without jamming) was determined using a 0–15 litre/minute Rotameter. The results are shown in Table 1.

These results show that the possibility of jamming when using a continuous flow would have been much less if a

Table 1.

Type of valve	Maximum flow without jamming (litres/minute)
Ambu Hesse valve	> 15
Ambu E valve	> 15
Penlon valve (prototype)	> 15
Laerdal III valve	3
Ambu Mk III resuscitator valve	3
Laerdal IV anaesthesia valve	2
Ambu MS valve	< 0.1

valve of the Ambu E or Ambu Hesse type had been chosen for the drawover modification of the Boyle's apparatus.

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I.T. HOUGHTON

A reply

Thank you for the opportunity to reply to the letters of Lieutenant Colonel Houghton and Major Tighe. It is clear that the adaptation of the Boyle's machine could be improved by using one of the valves suggested by Lieutenant Colonel Houghton in place of the standard Laerdal valve.

Dr Tighe suggests using a standard arrangement of the Triservice drawover system with oxygen added through the Rotameter of the Boyle's machine. This arrangement of the Triservice has been used in our hospital over the past 18 months when a higher flow of oxygen has been required than can be supplied by the Houtonox valve, which has a maximum output of 4 litres/minute.[1] The difference between this system and the drawover Boyle's machine is that a continuous flow anaesthetic is readily administered from the latter, and we consider that there are situations in which some anaesthetists may find this useful. We adapted the machine 18 months ago and it has since been used mostly in the continuous flow mode by our anaesthetists, although it is easily adapted for drawover. The problem with adopting the 23-mm taper system is that it would cause difficulties in using the vaporizer with other standard apparatus.

We are grateful to Dr Tighe for his suggestion about the reason for lightening of anaesthesia; another factor is that halothane, air and oxygen anaesthesia contains little analgesia which could have contributed to patient movement as well. We have also noticed this occasionally when using the standard Triservice apparatus without trichloroethylene.

Unfortunately we were unable to measure the $F\text{I}O_2$ since the equipment was not available, but it would be useful to do this. The internal volume of the backbar from Rotameter block to the common gas outlet is about 150 ml. When high flows of oxygen are used in the drawover mode a reservoir bag is probably essential to ensure a high concentration of oxygen in the system and it may be safer to do this as a routine.

We agree it is unfortunate that standard drawover apparatus is not used more frequently in developing countries. The reasons for this are often related to the little attention this type of equipment receives in centres of excellence in the developed world, and deteriorating economies making replacement of any apparatus difficult. It is also our experience in Zambia that some anaesthetists who trained with continuous flow apparatus are reluctant to use drawover equipment for certain cases. It is in this situation the drawover Boyle's machine may have a place.

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I.H. WILSON
J.R. SINCLAIR

Reference

1. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **46:** 1094–108.

Diclofenac and oedema

Drs Bone and Fell describe the use of diclofenac suppositories administered peroperatively to relieve pain after tonsillectomy (*Anaesthesia* 1988; **43:** 277–80). We consider that this drug is valuable, not only for pain relief, but also in the reduction of postoperative oedema. The preliminary results of a study of its use in adults undergoing rhinoplasty are encouraging.

Rhinoplasty presents problems of both postoperative pain relief and fixation of the nasal bones after their deliberate fracture and repositioning. The problem is to prevent the plaster of Paris from becoming loose as postoperative swelling first lifts it and then, as the swelling subsides, leaves it no longer a snug fit on the nose. The usual answer is to tape the nasal soft tissues with hypo-allergenic tape in an effort to reduce the swelling. There is often bruising and discoloration around the eyes even if this is successful.

The use of diclofenac peri-operatively has improved patient comfort and has much reduced the bruising around the nose and eyes. We hope to establish that this has rendered splintage of the mobile nasal bones more secure and may improve the eventual cosmetic result.

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D.J. WATSON
S.H. LAHIRI

Caudals and antisepsis

It is evident from Wildsmith and Armitage's response (*Anaesthesia* 1988; **43:** 514) to a comment made by Justins in his review of their book (*Anaesthesia* 1988; **43:** 158) that there remains some controversy over the avoidance of bacterial contamination during sacral epidural block.

It is pertinent to consider other potential sources of contamination whether gloves and gown are worn or not. The natal cleft is an inherently dirty area which harbours intestinal flora which can be transferred to the needle by the gloved or ungloved hand. Many anaesthetists employ routinely hyperdermic needles which are hollow, have a long sharp bevel, and may carry a core of skin tissue into the sacral epidural space. It is common for glass flakes to enter the liquid within when an ampoule is snapped.

These three risk factors can be minimised by modifications to technique. If, after skin preparation, an Op-site or similar adhesive transparent dressing is applied over the site, contact between hand or needle and the dirty area is prevented. A short spinal needle with trocar eliminates the risk of coring out skin. Local anaesthetic solution can be drawn up using a filter needle; this is preferable to the alternative of injection through a filter which eliminates the tactile feedback of low resistance to injection.

These techniques are my routine practice. None add much to the cost or time taken, nor do they detract from 'feel', and I commend them to all who employ this simple and useful block.

South Cleveland Hospital,
Marton Road,
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N. PUTTICK

Harness for use during anterior cervical fusion

Segments of bone are wedged into the interspaces between the vertebral bodies during anterior fusion of the cervical spine. The anaesthetist is asked to pull the head to distract the vertebral bodies to facilitate this manoeuvre.

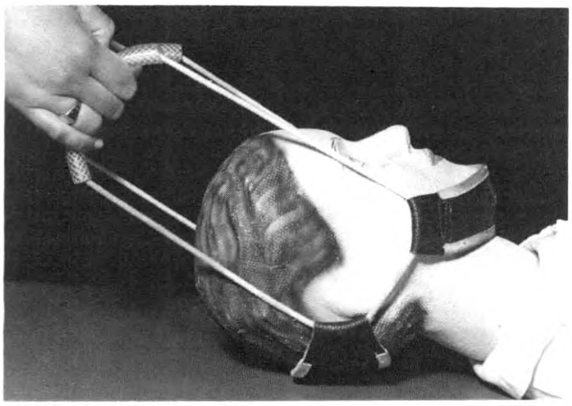

Fig. 1.

It is difficult to obtain adequate adhesion on the facial skin to apply traction; gripping the jaw can be difficult because it is close to the operative site; it is difficult if the patient has a fat neck, and it is a strain on the finger tips. The ears, while performing a very useful function, have severe limitations as handles for traction. With all these methods the force of the traction is variable, it is difficult to maintain, and there is the risk that the fingers may suddenly slip.

A simple adjustable harness was therefore developed (Fig. 1) which is put on before or after induction of anaesthesia. When traction is required, the anaesthetist pulls on the handles. This allows a controlled degree of traction to be maintained without difficulty for as long as is required by the surgeon. The direction of traction can also be controlled.

The harness was constructed by Mr Cairns of the Orthopaedic Workshop at the Princess Margaret Rose Orthopaedic Hospital in Edinburgh.

Princess Margaret Rose Hospital,
Edinburgh, EH10 7ED
E.L. Lloyd

Transient inability to see

The muscle pains after suxamethonium may be very unpleasant and if inflicted on daycase patients may cause unnecessary work for the general practitioner. A small dose of non-depolarising muscle relaxant injected several minutes before suxamethonium, may prevent fasciculation and muscle pains. However, the non-depolariser may produce noticeable effects before anaesthesia is induced, and these may prove distressing to the patient. We would like to relate an effect of which we were previously unaware.

One of the authors (J.E.P.) broke his nose which required manipulation under general anaesthesia. The other author administered 3 mg alcuronium intravenously several minutes before induction of anaesthesia and paralysis with suxamethonium. Dr Peacock stated, in answer to enquiry about the effect, that he could not see, although his eyes were open and there was no other evidence of muscular weakness. His vision was normal afterwards with neither other sequelae nor muscle pains.

An ophthalmic colleague supplied the explanation. Normally the eyes are in constant fine motion, small drifts and microsaccadic movements, to prevent fatigue of retinal cells by shifting the image. The small dose of non-depolarising relaxant was sufficient to prevent these movements; fatigue of the retinal cells and consequent blindness resulted.

Undue distress to the patient may be prevented by adequate warning of possible transient ocular side effects which may be induced by pretreatment with a non-depolarising muscle relaxant.

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Sheffield S10 2RX
J.E. Peacock
A. Padfield

Pain on injection of propofol

Scott *et al.* (Anaesthesia 1988; **43:** 492–4) in their recent communication, have demonstrated that the incidence of pain on injection of propofol was not diminished when propofol was administered through a fast-flowing intravenous infusion of 5% dextrose BP. This is in accordance with my own findings using a fast-flowing infusion of compound sodium lactate solution.

Eighty-six patients, aged between 21 and 76 years, ASA grades 1 and 2 were premedicated with temazepam 20 mg, and an 18-gauge Vygon cannula was inserted into the cephalic vein at the wrist, without any local infiltration. They were then assigned randomly to one of two groups: Group 1, no infusion; Group 2, a rapid infusion of compound sodium lactate was started. Propofol was injected at a rate of 2 ml/second and the incidence of pain was noted. There was no significant difference in the incidence of pain on injection of propofol between the two groups 23 and 27% respectively.

Queen's Medical Centre,
Nottingham NG7 2UH
M. Gamil

Anaesthesia, 1988, Volume 43, pages 996–998

Book reviews

Consciousness, awareness and pain in general anaesthesia 996
Edited by M. ROSEN AND J.N. LUNN
Aspects of recovery from anaesthesia 996
Edited by I HINDMARCH, J.G. JONES AND E. MOSS
Medicine for disasters 997
Edited by P. BASKETT AND R. WELLER
Respiratory emergencies 997
E.H. SAWICKA AND M.A. BRANTHWAITE
Books received 998

Consciousness awareness and pain in general anaesthesia

Edited by M. ROSEN AND J.N. LUNN. Pp. x + 195. Butterworths, 1987. £29.50.

This excellent book reviews all aspects of awareness during general anaesthesia. The contributors include psychologists, lawyers and anaesthetists from both sides of the Atlantic. The subject is of particular importance at present because of increased litigation in the United Kingdom after a successful suit brought by a patient who experienced pain during Caesarean section. The book was produced after a workshop had considered the problem, but does not comprise simply the proceedings of that meeting.

The introductory chapters describe the continuum of anaesthesia, the importance of ensuring lack of consciousness during surgery and the difficulties of interpreting the clinical signs of anaesthesia. Monitoring techniques which are claimed to supplement clinical signs, including processed and unprocessed electroencephalography, electromyography and oesophageal contractility, are discussed at length; inevitably, the investigators who describe their work are rather more optimistic about its clinical value than might be the objective reader, but there can be no doubt that research in this field has contributed significanlty to our understanding of the processes of memory and consciousness during anaesthesia.

Three chapters describe various aspects of cognitive function during general anaesthesia, a process which is of course related to recall of intra-operative events, but which is linked also to the phenomenon of 'unconscious perception', whereby auditory material presented during anaesthesia may be recognised, or may alter the patient's behaviour, at a later time.

The medicolegal sequelae of awareness are discussed at length. In contributions by an anaesthetist and lawyers from both sides of the Atlantic, the common causes of awareness in cases that have led to litigation are described, and the anaesthetist's responsibilities defined. Interestingly, law suits related to awareness during anaesthesia appear to be much commoner in the UK than in the USA. The importance of record-keeping, and honesty and communication with the patient who claims to have been aware, are stressed.

There is an appendix which details the experiences of 27 patients who answered an advertisement seeking individuals who were conscious during surgery. Their comments, which are not coloured by bitterness or the prospect of financial compensation, should be read by every practising anaesthetist.

It is unfortunate that medicolegal pressures have been required to excite general interest in awareness. The fact that the anaesthetist fails in his or her duty to ensure unconsciousness in up to 1% of paralysed patients should have attracted more attention many years ago. The subject of awareness ought to be of paramount importance to all anaesthetists. It is clear that the potential for awareness will continue to exist for some time, but that care in clinical practice provides the most efficient method of prevention at present. The editors of this book have been successful in combining all aspects of the subject in a form which will stimulate all anaesthetists, whether their interest is clinical, academic or merely defensive.

A.R. AITKENHEAD

Aspects of recovery from anaesthesia

Edited by I. HINDMARCH, J.G. JONES AND E. MOSS. Pp. xii + 176. John Wiley, 1987. £23.50.

This volume is a compilation of papers presented at a small conference hosted by the University Department of Anaesthesia in Leeds to discuss the residual effects of drugs administered by the anaesthetist on patients who have undergone daycase surgery. A more specific title could have been selected for the book.

The major proportion of the book deals with recovery of memory, and cognitive and psychomotor function, after daycase surgery. The introductory chapters discuss the subject of daycase surgery more generally, with anecdotal accounts by an anaesthetist and a surgeon. There follows a series of accounts of recovery after daycase surgery undertaken using a variety of anaesthetic techniques; these chapters vary from descriptions of the results of original research to short review articles. Hidden inexplicably in the midst of these offerings is one of the most interesting chapters in the book, describing ventilatory control during recovery from anaesthesia. Unfortunately, the major conclusions of this chapter, that opioids are the major contributor to hypoxaemia in the postoperative period and that patient-demand analgesia must be used with caution, appear rather out of place in a book describing the effects of anaesthesia for daycase surgery.

Propofol is now recommended widely for use in daycase surgery, but this agent was presumably not readily available at the time of the conference, as it warrants less than three pages in a chapter that reviews only six publications, the account of a comparison with methohexitone in respect of memory after daycase surgery and a few sporadic comments in chapters that deal predominantly with other drugs. The importance of residual sedation and amnesia after benzodiazepine administration are highlighted in a review chapter, and the effects of these drugs on anxiety and psychomotor function are described in an account of two small investigations.

These contributions, which are mixed both in quality and sequence, are the fat round the meat of the book, which is the discussion by acknowledged experts of the effects of anaesthetic drugs on mental function, and methods by which these effects may be assessed. There are excellent chapters describing the complexities of memory and the duration of postanaesthetic mental impairment, and an exhaustive account of the various methods which have been used to assess these variables after anaesthesia, together with a critical assessment of their relative sensitivities. There is a 39-page appendix which lists virtually all the publications on this topic, the methods of assessment used and the results elicited.

Inevitably, books which seek to publish the proceedings of a conference contain chapters with a wide variety of style, scientific merit and intellectual interest. The variety in this book is considerable, and is not helped by lax editing. As alluded to already, the title may be rather misleading. However, for those with an interest in recovery of mental function following daycase surgery, the major contributors to the book have provided a valuable source of reference material.

A.R. AITKENHEAD

Medicine for disasters

Edited by P. BASKETT AND R. WELLER. Pp. xviii + 494. John Wright, 1988. £60.

Books are often published with the claim that they are new to the field and that they fill a gap. In most cases this is only half true but to my knowledge, this book really is the first of its kind.

The editors have assembled the expert knowledge of some of the best known writers in the field of disaster medicine from all of the best known writers in the field of disaster medicine from all over the world. As might be expected, these are heavily weighted towards North America and the medical services (armed services, ambulance services etc.) of a number of countries but members of BASIC (British Association for Immediate Care) are well represented.

The objectives of the book are to present data on the immediate responses which are needed to any disaster, natural or man made. These include earthquakes, fires, floods and the escape of toxic chemicals. The historical introductory section is followed by three chapters concerned with the medical requirements for triage, resuscitation and anaesthesia. This last is very sensible and practical. The reader may be unfamiliar with the Tri-Service Anaesthetic apparatus which is referred to extensively, but this is obtainable commercially, or may be assembled from its individual parts. It is interesting to read of the rebirth of open chest cardiac massage in one of these sections.

Most of the rest of the book is devoted to a discussion of planning and management. The planning section describes the differences in the methods which are available in developed and less developed countries. All the chapters are very clearly presented, but that on Disaster Planning in Developed Countries is particularly informative and useful. The same author later provides a chapter on Public Relations and the Media which demonstrates the value of providing a formal communications team in any major disaster plan. The subsequent sections, which concern the problems of underdeveloped countries, demonstrate just how difficult it is to perform efficiently under unexpected circumstances.

Many of these sections are a rather uneasy combination of general planning and specific detail and lists, tables and flow charts. The latter are very popular but I regret to say that I find them rather confusing. This particularly relates to a series of four charts on the various stages of triage. These presumably represent logical processes which the trained rescue worker has acquired but they are not easy to follow.

A very large amount of the clinical information was new to the reviewer and all the more welcome for that. There was a very readable section on the psychological response to disasters and it was instructive to learn that major upheavals are not commonly followed by epidemics.

The final section deals in detail with specific natural and man-made disasters including the consequences of civil strife, and the book is completed by a useful directory of the organisations which may need to be mobilised to deal with any such eventuality. The book is very solidly produced and clearly printed with some interesting photographs, as well as the diagrams and tables referred to earlier. I have grave doubts as to the need and purpose of the rather extensive biographical detail provided for the many contributors but it is arguable that such a provision allows the reader to know upon what authority the various sections are written.

Overall the book has fulfilled its apparent objectives and I think it will become a standard reference text for anyone involved in the organisation and planning for disaster on either a small or a large scale. In addition to anaesthetists and others who share responsibility for hospital disaster planning these will include the ambulance and rescue services, the police force and members of the armed services.

J.C. STODDART

Respiratory emergencies

E.H. SAWICKA AND M.A. BRANTHWAITE. Pp. 88. Butterworths, 1987. £7.95.

This pocket-sized book contains 10 chapters. The first discusses in general terms the diagnosis, assessment and investigation of respiratory failure, and the other nine deal with the diagnosis and management of nine categories and resporatory emergency, that range from specific entities such as asthma, to groupings such as upper airway obstruction or pneumothorax, lung cysts and bronchopleural fistulae. It aims to provide immediate guidelines and information for junior medical staff who provide emergency treatment for patients suffering such illnesses.

The authors admit that because the book is condensed, the contents might be viewed as didactic and sometimes controversial, and this is indeed so. Nevertheless much good common sense and caution is included. Some is pertinent (for instance which pneumothoraces one should not drain) while some relates to decisions one hopes are taken by senior staff (for instance which patients may be viewed as terminally ill and thus not receive controlled ventilation of the lungs).

Some parts of the book are more up-to-date than others; almitrine, a drug which is as yet available only on a named patient basis, is included but, on the other hand, the section on management of ARDS excludes several recent theories.

The concise nature of the book leads to statements of facts without explanation, and one wonders whether a little enlargement would make the details easier to remember, or whether this would only serve to deter the casual reader. Tables and figures are present in good measure, and the tables of differential diagnoses are particularly clear and useful. The ECG illustrations do not have the abnormality described specifically, and thus lose some of their value.

There are no references, but a short reading list of four textbooks is included, although not all the editions cited are current. The index is well laid out and comprehensive, an important point in a book designed for quick reference. The intended readership includes junior staff in Medicine and Accident and Emergency; anaesthetists in Intensive

Care; and doctors studying for MRCP, FFARCS and FRCS examinations. It will prove a useful handbook for those in the first group. Most examinees will already know most of the information contained, but the book may prove a helpful *aide-memoire*.

N.D. GROVES

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We thank the publishers for the following books which may be reviewed in future issues of *Anaesthesia*.

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R.D. DRIPPS, J.E. ECKENHOFF AND L.D. VANDAM. Pp. x + 499. W.B. Saunders, 1988. £18.50.

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D.R. BEVAN, J.C. BEVAN AND F. DONATI. Pp. x + 443. Year Book Medical, 1988. £37.50.

Anaesthesia, 1988, Volume 43, pages 999–1002

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The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

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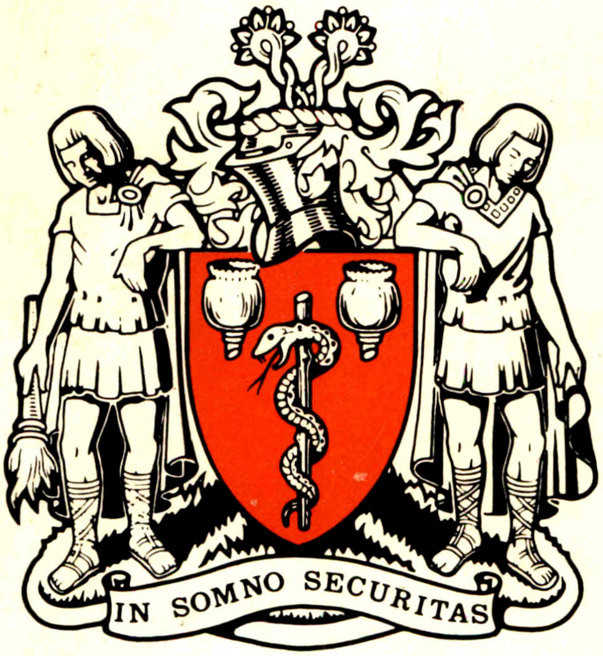

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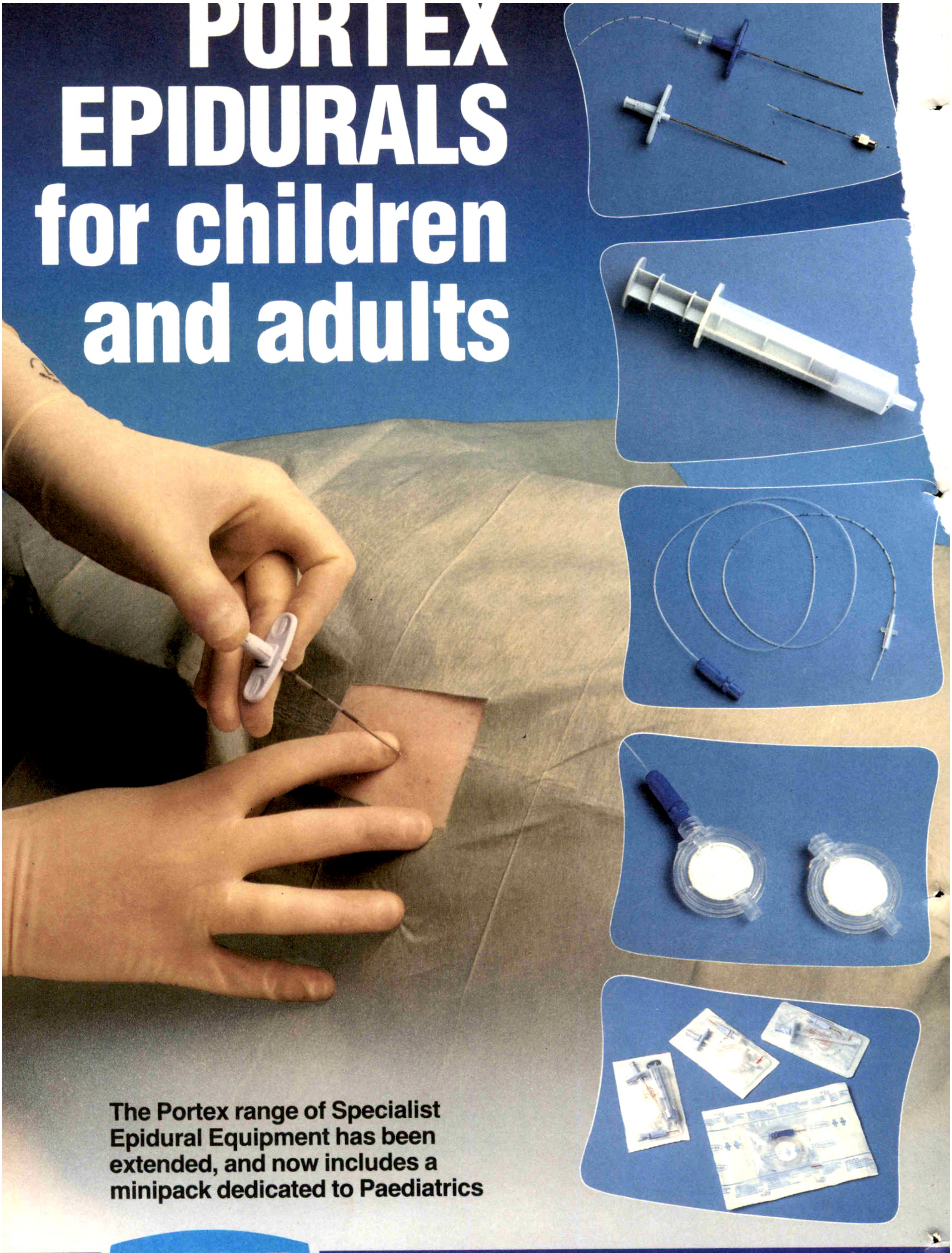

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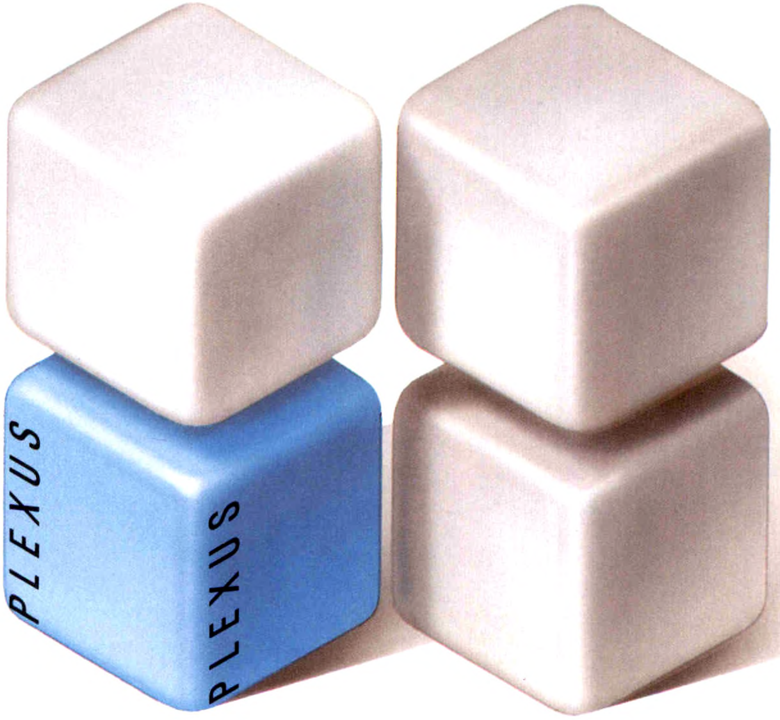

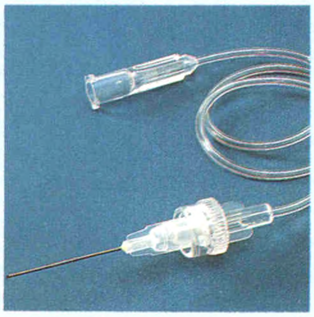

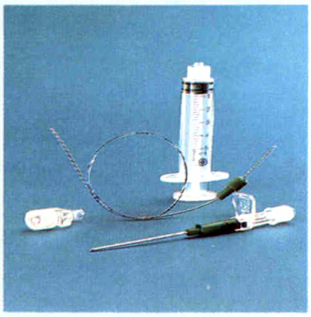

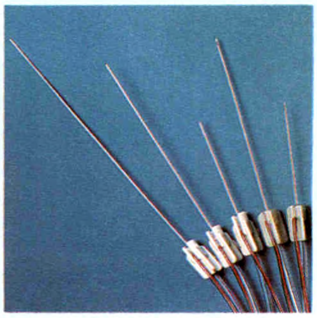

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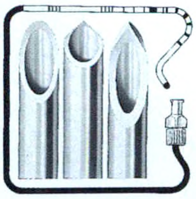

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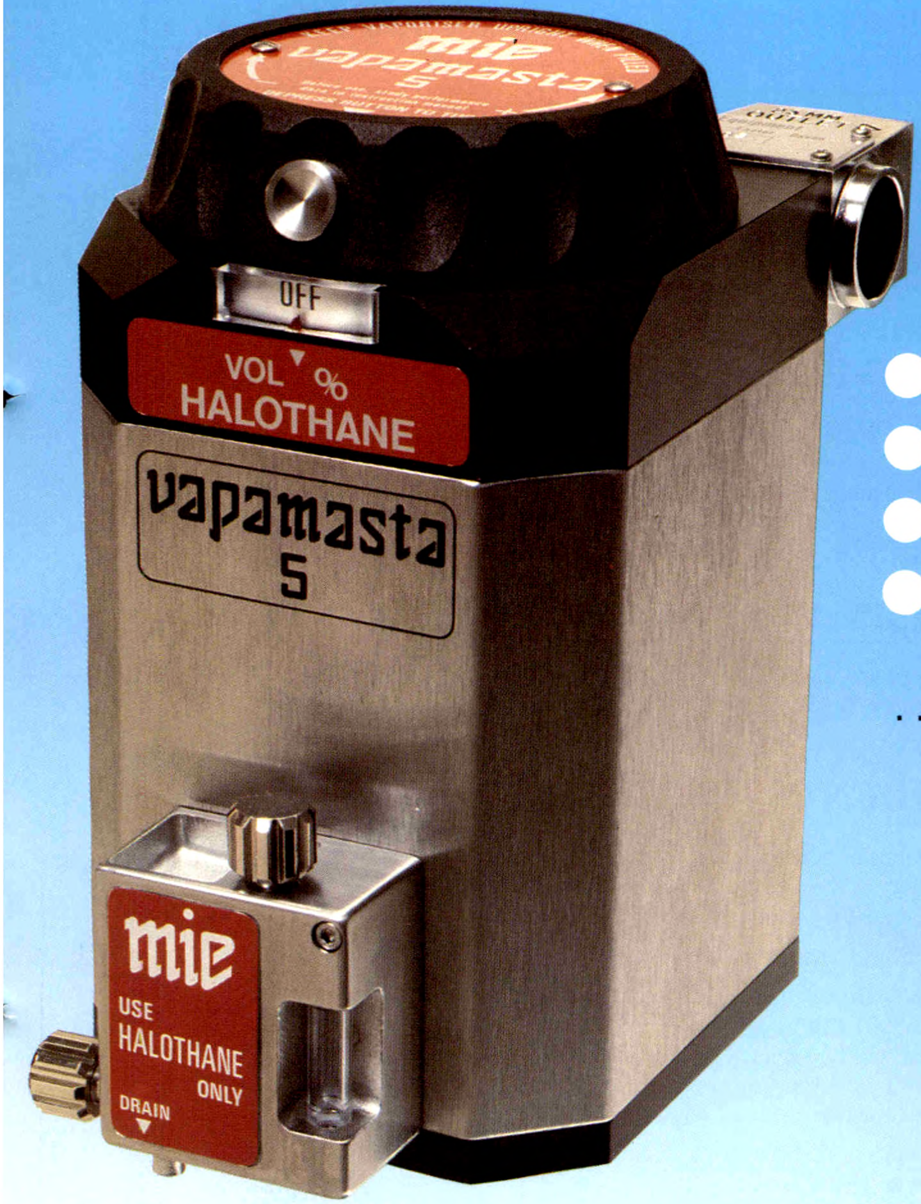

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Anaesthesia, 1988, Volume 43, pages 1003–1004

Editorial

Arrhythmia prevails

A dozen or so years ago, a minor battle raged in the cardiological journals about the correct word to define disorders of cardiac rhythm. To all intents it has been resolved, but occasionally one still sees the usage dysrhythmia, with the implication of greater precision in definition offered by the author. What's in a name, one might ask? Perhaps a few points about the choice of names might be relevant here.

Neologisms are the order of the day when techniques develop, or diseases are described that were not recognised previously, and the like. Eponyms may suffice at first, but usually there is early recognition of the need for an anatomically or physiologically based description that will be meaningful to the uninitiated, and equally valuable to those in the know, so that they can be sure that each means the same. Perhaps a good example here, which illustrates the technical factors that finally determine the use of words, will emerge from a brief review of the development of balloon techniques for the dilatation of stenosed cardiac valves. The authorities who have commented on the techniques of coronary angioplasty dislike the word that has been attached to it, and question its correctness,[1] yet this has taken hold, and is so widely accepted that it would be futile to attempt to reverse the trend by insistence on greater etymological precision.

We do, however, now run into a problem when it comes to balloon dilatation of valves, and indeed of arterial stenoses elsewhere. It is wise to turn to the National Library of Medicine of the United States to seek guidance, for they determine the medical subject headings (MeSH), which are recommended to indexers, and which are the descriptors favoured by their standard publication, *Index Medicus*. They seek advice from various consultants, with expertise in linguistics as well as medicine, and see whether single-word descriptors can be devised. Unfortunately many of these are destined never to catch on; they are clumsy and by no means euphonic. Balloon valvuloplasty is very popular in this specific case, but a substantial majority of British cardiologists would prefer to say balloon valvotomy. Perhaps even more would be happy with the decision taken by the National Library of Medicine, to whose Thesaurus Development Specialist, Mrs Sally Davidson, I am indebted for guidance and explanation. Their decision has been to stress the general concept, so they provide the 'dilatation' aspect with a generous supply of more specific entry terms. Balloon dilatation[2] is thus recommended as the description of nonoperative repair of occluded vessels, ducts or valves by a balloon catheter: subheadings, more specific, include balloon catheterisation, tamponade and valvuloplasty. Indexing should always be borne in mind by the author who wishes to see his paper quoted; time will tell, however, and I suspect that balloon valvuloplasty will prevail. Then the Medical Subject Heading Section will respond to evidence of the requirements of authors and editors, which are as vital to the development of small medical subject headings as are those of searchers and indexers.

What about older terms which might then turn out to be wrong? Here we generally allow ourselves to be saddled with them, because they have been with us and have proved useful friends, with accepted meanings. Every now and then, however, an old friend is reviled and an attempt made to replace it with something better. When there is reason, there may be justice; where it is founded on a misconception, only misunderstanding can result.

The earliest modern description of a general term for disorders of cardiac rhythm that I have been able to locate appeared in 1889 in a treatise by Germain Sée.[3] He described such disorders as arrhythmias, when the pulse was totally irregular, and allorhythmias, when the pulse had a repetitive form to it but was not precisely regular. These terms depended substantially on the simple clinical tools of palpation of the pulse and auscultation of the heart, with limited supplementation by early graphic techniques then being developed. That arrhythmia served a useful purpose and was meaningful is indicated by the fact that it was adopted forthwith by early pioneers of its study, all of whom had classical educations; thus, in the last decade of the 19th century, it became the natural word used by cardiologists whose tongue was Germanic (Karel Frederik Wenckebach) and English (Sir James Mackenzie) as well as French (Sée and his successors including Henri Vaquez). The next generation, that included Sir Thomas Lewis, Paul Dudley White, Frank Wilson, and others from the continent, had no doubt that arrhythmia meant an abnormality of the cardiac rhythm. But we have even older precedent for the use of arrhythmia in this sense, for some 1800 years ago this was the choice of Galen himself.[4] Galen (AD 132–201) described irregularities of the intermittent pulse as the most dangerous, possibly producing sudden death. He defined the normal pulse relations as eurhythmus, and abnormal time relations caused the pulse to be arhythmus. He divided arhythmic (*sic*) pulses into three varieties according to the degree of deviation from eurhythmus and it is quite clear at no stage did he ever consider that arhythmus meant absence of pulse activity.

The word dysrhythmia appeared for the first time in the *British Heart Journal* in 1967.[5] The authors had previously used arrhythmia for the same purpose but considered that arrhythmia was unclear and meant absence of rhythm; 'largely to express with more certainty that a difference does exist between a completely absent heart beat, e.g. asystole or even ventricular fibrillation, and a heart beat that might be inappropriate but still had a natural rhythm, we began using the term "dysrhythmia"' (Leon Resnekov, personal communication, 3 November 1981). This came in for heavy criticism by Cornelio Papp,[6] for reasons akin to those given now. Scherf and Schott likewise felt that 'absence of physiologic rhythm' was best expressed by the term arrhythmia.[4]

The World Health Organisation and International Society of Cardiology set up a task force in 1976 on terms related to

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cardiac rhythm and had no problems in choosing arrhythmia to define 'any cardiac rhythm other than normal sinus rhythm. Such a rhythm may be either of sinus or ectopic origin, and either regular or irregular. An arrhythmia may be due to a disturbance in impulse formation or conduction, or both'.[7] Even earlier, in 1973, Walter Somerville, my predecessor as editor of the *British Heart Journal*, had misgivings about the use of dysrhythmia and consulted Dr Donald Russell of the Department of Greek at Oxford University. He distinguished between 'a(n)—' which is simply a negative, and 'dys', which gives the idea of difficulty or disagreeableness. He thought that arrhythmia covered the patterns described by cardiologists best and also stressed the fact that arrhythmos and its relatives were well attested in ancient Greek, whereas dys– compounds were not. The attested senses of the *arrhythmos* words were interesting, he said, and conveyed not absence of movement but lack of shape or pattern. The analogy he gave was that arrhythmos was used with walking in the sense that it indicated walking out of time or out of step. He felt 'that *arrhythmia* will do very well for an irregularly beating heart . . .'

Both Dr Somerville and I were impressed by the classical arguments, and fortified by the knowledge that previous generations of cardiologists and physiologists, accustomed to dealing with classical languages, had found it acceptable. Asystole would certainly do for the cessation of activity of the heart, and there seems to be no need for a separate descriptor of disturbance of arrhythmia on the analogy that arrhythmia could be meant or should be taken to represent lack of activity. Again to quote Russell's personal communication: '. . . and to use *arrhythmia* for cessation of movement seems really misleading.'

Dysrhythmia seemed to catch on as a vogue word, but it was curious to see how often those who espoused it also used the word arrhythmia in the same paper, clearly interchangeably; and when it came to indexing papers and their titles, it was a self-defeating exercise to have two separate entries for the same meaning, for it would then be very easy for someone consulting the index to miss another set of papers, listed under a different heading. The classical heading prevailed, and with rare exceptions cardiologists continue to use the term with this understanding. Arrhythmia is indeed the *Index Medicus* subject heading, not dysrhythmia.

Since I reviewed some of these aspects, advocating the usage 'arrhythmia',[8] I have questioned about 300 consecutive patients who visited England from Greece, complaining of pulse abnormalities. They have consistently used the term tachycardia to mean a rapid pulse and arrhythmia to mean an abnormal, irregular pulse, usually rapid but sometimes slow. None of them has ever volunteered the use of the term dysrhythmia, and, when asked whether dysrhythmia might be an alternative acceptable to them, none thought it appropriate. Such agreement between classical and modern Greek usage, the principles of medical etymology, and the longstanding definition of arrhythmia that had never previously troubled our cardiological forefathers, persuade me that we should continue to talk of arrhythmia.

All this is now almost historical for we have for so many years been able to classify arrhythmias more precisely with the electrocardiograph or with more sophisticated recording techniques. When there could have been a major debate, there was none; and arrhythmia has a very general and well accepted meaning, while we are better able to define specific arrhythmias by their proper descriptors, e.g. atrial fibrillation, paroxysmal supraventricular tachycardia, etc. Clarity should prevail, and it would be graceful to see *Anaesthesia* agree that established words are not necessarily wrong ones, and that good reason exists for the preference for arrhythmia as well as the lack of need for dysrhythmia.

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Editor's note

The Editors are convinced by the arguments above and from Vol. 44 onwards our recommended term is arrhythmia and we are particularly grateful to Dr Krikler for his gentle correction.

Editorial notices

Anaesthesia News

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Intra-ocular pressure changes during rapid sequence induction of anaesthesia

A comparison between thiopentone and suxamethonium and thiopentone and atracurium

L. EDMONDSON, S. L. LINDSAY, L. P. LANIGAN, M. WOODS, AND H. E. R. CHEW

Summary

The changes in intra-ocular pressure associated with two different anaesthetic induction and tracheal intubation techniques were compared ($n = 30$). After pre-oxygenation, Group A received thiopentone (5 mg/kg) followed by suxamethonium (1.5 mg/kg), both within 25 seconds, and Group B atracurium (0.5 mg/kg) followed by thiopentone (5 mg/kg) again both within 25 seconds. Tracheal intubation occurred after one minute in Group A and 2 minutes in Group B to allow for full paralysis. In Group A intra-ocular pressure did not alter significantly from baseline and the maximum increase was only 0.93 mmHg. The statistical type II error risk was consistently below 55% and all 95% confidence limits included negative values. Intra-ocular pressure in Group B was consistently lower than baseline ($p < 0.05$) but with a longer induction–intubation interval. These results therefore provide valuable information about the 'balance of risks' when choosing a muscle relaxant for an inadequately starved patient with a penetrating eye injury.

Key words

Anaesthesia; ophthalmic.
Neuromuscular relaxants; atracurium, suxamethonium.

Patients with penetrating eye injuries may present for surgery with a potential full stomach and in this situation many anaesthetists would choose a rapid sequence induction. Suxamethonium remains the relaxant of choice for this technique, but its use is accompanied by an increase in intra-ocular pressure (IOP).[1–3] A number of studies[4–7] have investigated the substitution of atracurium or vecuronium for suxamethonium. However, this has not eliminated increases in IOP above baseline values[4,5] and is associated with other disadvantages. These are an increased delay in obtaining full relaxation;[6,8,9] suboptimal intubating conditions;[9–11] administration of the relaxant 20–30 seconds before induction,[7–12] and a lowered safety margin in failed intubation. One previous paper only[12] has compared the IOP changes when suxamethonium or atracurium was used for rapid sequence induction. The authors confined their conclusions to the suitability of atracurium in rapid sequence induction but there was evidence that suxamethonium could be associated with only minimal elevations in IOP. Our study therefore further investigates the changes in IOP when thiopentone and suxamethonium or thiopentone and atracurium are used for induction and intubation.

Methods

Thirty patients in ASA groups 1 or 2 and aged 16–65, who required tracheal intubation for nonophthalmic surgery were included in the study; all gave informed consent which had ethics committee approval. Hypertensive patients and those with known ocular disease were excluded. Premedication was with papaveretum 0.3 mg/kg and hyoscine 0.06 mg/kg intramuscularly one hour before anaesthesia. Baseline IOP, arterial blood pressure and pulse were recorded on arrival in the anaesthetic room. Baseline IOP was measured in the right eye with the patient supine, using a Perkins hand-held applanation tonometer.[13] All readings were taken after the topical instillation of lignocaine and flourescein eye drops and performed by one of the authors (L.L.), who was unaware of the anaesthetic agents used. All patients were pre-oxygenated for 2 minutes before induction and allocated randomly to one of two groups.

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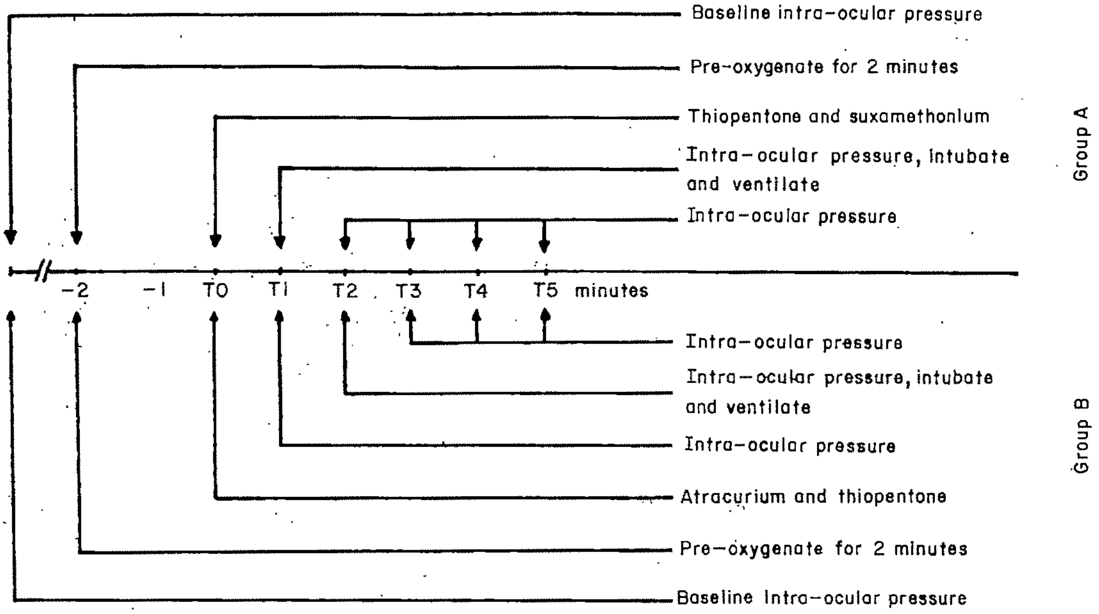
Baseline intra-ocular pressure
Pre-oxygenate for 2 minutes
Thiopentone and suxamethonium
Intra-ocular pressure, intubate and ventilate
Intra-ocular pressure
Group A
-2
-1
T0
T1
T2
T3
T4
T5
minutes
Intra-ocular pressure
Intra-ocular pressure, intubate and ventilate
Intra-ocular pressure
Atracurium and thiopentone
Pre-oxygenate for 2 minutes
Baseline intra-ocular pressure
Group B

Fig. 1. Group A received thiopentone 5 mg/kg and suxamethonium 1.5 mg/kg, both within 25 seconds. Group B received atracurium 0.5 mg/kg and thiopentone 5 mg/kg, both within 25 seconds.

Group A received thiopentone 5 mg/kg and suxamethonium 1.5 mg/kg at time 0. Induction was completed within 25 seconds and IOP was measured at 1, 2, 3, 4 and 5 minutes (Fig. 1). Intubation followed the one-minute reading in order to allow for full paralysis. Group B received atracurium 0.5 mg/kg followed by thiopentone 5 mg/kg at time 0. Again, induction was completed within 25 seconds and IOP was measured at 1, 2, 3, 4 and 5 minutes, (Fig. 1). Intubation followed the 2-minute reading in order to ensure adequate relaxation.[6,8]

The presence of any coughing at intubation was noted. Once intubated, all patients' lungs were ventilated by hand using a Bain-type breathing system (Mapleson D). Anaesthesia was maintained with 0.5% halothane in 70% nitrous oxide and 30% oxygen. Fresh gas flow was 70 ml/kg to equalise the effect of carbon dioxide on IOP. Heart rate and blood pressure were measured at the same time as IOP by the electrocardiogram and the Riva Rocci method respectively.

Statistical analysis

Baseline values were used as the reference point for all statistical analysis. Within-group changes in IOP, blood pressure and heart rate were analysed using the paired *t*-test and between-group changes using the *t*-test. Individual instead of group changes were used for IOP as this reduces the type II error, particularly when a parameter shows large individual variation (i.e. IOP).[14] (A type II error is the risk of there being a difference between the groups when the results actually show no statistical difference). The different time sequences for intubation means that T2–T0 in Group A was compared with T3–T0 in Group B etc. The Bonnferroni correction was applied because of multiple comparisons.

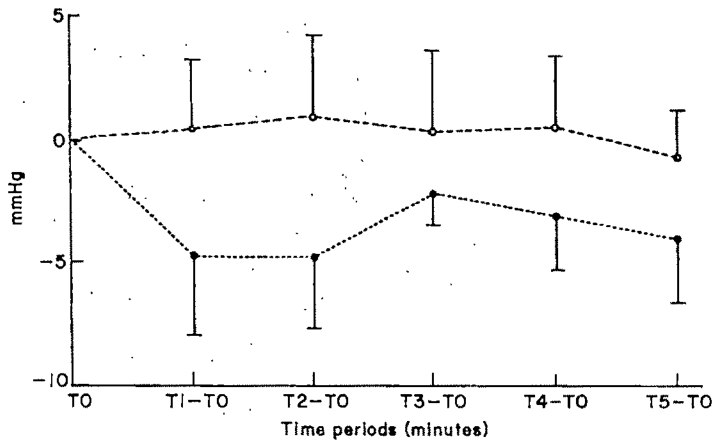

Fig. 2. Mean (SD) of individual changes in intra-ocular pressure relative to baseline. ○, Group A; ●, Group B. Intubation occurred after the T1 intra-ocular pressure reading in Group A, and the T2 reading in Group B.

The 95% confidence limits and type II error (see Appendix) were assessed where applicable. The null hypothesis was that there was no difference in IOP between the two treatment groups.

Results

There were no significant differences between the two groups for age, weight, baseline IOP, blood pressure and pulse (Table 1).

Within group changes in IOP

Mean IOP in Group A was marginally greater than baseline for four out of the five time periods (Fig. 2). The maximum mean increase in IOP was only 0.93 mmHg (Table 2). These increases were not statistically different from baseline. The type II error (see Appendix for details) ranged from 9% for the T1–T0 IOP to 55% for the T5–T0 IOP (Table 2). The 95% confidence limits for Group A are shown in Table 2. Each confidence limit includes a negative value. Mean IOP in Group B was consistently lower than baseline IOP ($p < 0.01$). The maximum and minimum decreases in IOP were 4.8 mmHg at T1–T0 and 2.2 mmHg at T3–T0 respectively (Table 2) (Fig. 2). The 95% confidence limits for Group B are shown in Table 2. Each confidence limit includes two negative values.

Between group changes in IOP

Mean IOP in Group B was consistently lower ($p < 0.05$) than Group A (Fig. 2). The maximum difference in mean IOP was 4.67 mmHg at T1–T0 but had decreased to 3.13 mmHg for the postintubation IOP (Table 2). The 95% confidence limits are shown in Table 2 and do not include negative values.

Systolic blood pressure and heart rate

The changes in systolic blood pressure and heart rate are shown in Table 3. Heart rate in Group A, rose significantly ($p < 0.05$) above baseline after intubation, with increases of 29, 27 and 20% for T2, T3 and T4 respectively. In Group B heart rate also rose significantly ($p < 0.05$) following intubation with increases of 21% for T3 and T4. The peak increases in systolic blood pressure were 8 and 12% respectively in Groups A and B. The rises in Group B just reached statistical significance ($p < 0.05$). There were no statistically significant differences between the two groups in terms of heart rate or systolic blood pressure.

Discussion

Traditional teaching has for many years recommended the avoidance of suxamethonium in patients who present with penetrating eye injuries. This advice is still supported by the manufacturers[15] and recent editions of standard textbooks of anaesthesia.[16–18] Their recommendation is based on previous work which demonstrated an increase in IOP with suxamethonium and included data from animals;[2,19] awake volunteers;[1] and patients during stable anaesthesia.[2–4,20] However, these studies do not represent the IOP changes during rapid sequence induction; the very situation in which suxamethonium is most beneficial. One recent paper[12] has studied the IOP changes of suxamethonium in this situation and compared them with those of atracurium. The study provided evidence of minimal rise in IOP with suxamethonium, but the authors only made recommendations on the suitability of atracurium in rapid sequence induction. Other authors who have used atracurium or vecuronium in this situation have failed always to

Table 1. Demographic data of patients studied. Values expressed as mean (SD).

	Group A (n = 15)	Group B (n = 15)
Age, years	37.0 (16.3)	39.6 (14.0)
Weight, kg	61.8 (7.8)	64.0 (11.2)
Baseline intra-ocular pressure, mmHg	13.0 (3.1)	14.1 (2.4)
Baseline systolic blood pressure, mmHg	122 (18.3)	126 (28.0)
Baseline pulse rate, beats/minute	72 (9.9)	73.4 (14.0)

Table 3. Data for heart rate and systolic blood pressure for Groups A and B. Values expressed as mean (SD).

	Heart rate (beats/minute)		Systolic blood pressure (mmHg)	
	Group A	Group B	Group A	Group B
T0	72 (9.9)	73.4 (14.0)	122 (18.3)	126 (28.0)
T1	84 (17.4)	80 (14.2)	121 (15.1)	120 (20.5)
T2	93 (13.5)*	80 (11.1)	132 (18.1)	115 (23)
T3	91 (15.9)*	89 (16.4)*	132 (19.5)	142 (31.3)†
T4	86 (17.5)*	89 (13.4)*	128 (22)	140 (23) †
T5	83 (14.6)	86 (14.5)*	126 (24.4)	127 (22.5)

* Significant increase compared with baseline ($p < 0.05$).
† Significant increase compared with baseline ($p < 0.05$).

Table 2. Individual changes in intra-ocular pressure (IOP, mmHg) with respect to baseline (T0). Values expressed as mean (SD).

	T1–T0	T2–T0	T3–T0	T4–T0	T5–T0
Group A (mmHg)	0.2 (2.8)	0.93 (3.3)	0.33 (3.3)	0.53 (2.8)	− 0.73 (2.9)
Type II error	9%	45%	30%	43%	55%
95% confidence limits	− 2.0, 2.4	− 1.5, 3.4	− 2.1, 2.8	− 1.6, 2.7	− 2.9, 1.5
Group B (mmHg)	− 4.7*† (3.4)	− 4.8* (2.9)	− 2.2*‡ (2.3)	− 3.13*† (2.2)	− 4.0*† (2.6)
95% confidence limits	− 7.2, − 2.2	− 7.0, − 2.0	− 4.9, − 0.5	− 4.8, − 1.5	− 5.9, − 2.1
Group A with Group B	T1–T0 T1–T0	T2–T0 T3–T0		T3–T0 T4–T0	T4–T0 T5–T0
95% confidence limits	2.5, 7.2	1.0, 5.3		1.4, 5.6	2.5, 6.5

* Significantly lower IOP than baseline ($p < 0.01$).
† Significantly lower IOP compared to Group A ($p < 0.01$).
‡ Significantly lower IOP compared to Group A ($p < 0.05$).

obtain improvements in either technique or IOP. For example, it has been necessary to administer the relaxant 20–50 seconds before induction,[4,7,12] in order to avoid prolonging the induction–intubation time or coughing on intubation. In addition, postintubation IOPs can increase to levels higher than baseline IOP,[4,5] because laryngoscopy alone is a potent elevator of IOP.[21,22] Therefore, there is inconclusive evidence that the present alternatives to suxamethonium offer major advantages for the patient.

The intention of this study was to clarify the balance of advantages and disadvantages when using suxamethonium or atracurium for intubation. The central aim of any anaesthetic technique in ophthalmic surgery is to limit increases in IOP. Coughing during intubation can lead to rises in IOP four times greater than those due to suxamethonium.[23] It is essential therefore to intubate only once the patient is fully paralysed. This will be after approximately 60 and 120 seconds respectively using suxamethonium (1.5 mg/kg) and atracurium (0.5 mg/kg).[6,8] For intubation to occur simultaneously in Group A and B it would be necessary to administer the atracurium 60 seconds before induction; a situation for which the authors felt unable to obtain informed consent. Intubation therefore occurred 120 seconds after induction in Group B. This doubled the induction to intubation time in Group B, but it is a logical approach when the principal aim is to avoid excessive increases in IOP.

The results obtained in this study indicate that, when thiopentone and suxamethonium are administered as part of a rapid sequence induction, IOP remains remarkably stable. The mean increase of IOP in Group A was 0.2 mmHg at one minute, with a maximum rise of only 0.93 mmHg at 2 minutes. Intra-ocular pressure then proceeded to decrease and by 5 minutes there was a fall in IOP of 0.76 mmHg. No increase reached statistical significance. These IOP changes significantly contrast with the rises of 7–8 mmHg previously documented with suxamethonium.[2,4,24] The differences found here can only be explained by the fact that the previous papers studied the IOP changes of suxamethonium in isolation, whereas this paper investigated the 'dynamic' situation of rapid sequence induction. Our results are also compatible with the only previous study,[12] where the maximum mean increase in IOP with suxamethonium was 3 mmHg. The lower mean rise obtained in our study is probably related to the differences in method, that is in the previous study a variable dose of fentanyl was given before induction and the speed of injection of thiopentone was not controlled; both of which will influence IOP.

It is important to assess the risk of overlooking a significant increase in IOP,[25] that is a type II error, in view of the sample size and lack of significant change in IOP in this study. The authors were able to achieve this (see Appendix and Table 2) and in combination with the 95% confidence limits added statistical validity to the results.

Intra-ocular pressure in Group B was consistently lower than Group A, but it was with the disadvantage of a longer induction to intubation time. This may be unacceptable in an inadequately starved patient. The alternatives, to administer the relaxant while awake or risk coughing on intubation, may also be unacceptable to the patient or to the maintenance of a low IOP.

Thiopentone is known to cause a profound decrease in IOP.[26] Therefore when injected rapidly and in adequate dosage, it may counteract the hypertensive effect of suxamethonium and intubation on IOP.[27] This could be the explanation for the lack of significant increase in IOP obtained in Group A.

A further factor that has precluded the use of suxamethonium is its induction of tonic contractions in the extra-ocular muscles.[2] This was first documented in 1955[2] but subsequent work in 1957[28] demonstrated that these contractions are abolished by thiopentone. Additional evidence does exist to support the potential for stable IOPs when suxamethonium is used in rapid sequence induction. Both Libonati[29] and Donlon[30] have reported retrospectively on a combined total of 900 cases of penetrating eye injury where suxamethonium caused no further damage to the eye.

In conclusion, this study has demonstrated that when thiopentone (5 mg/kg) and suxamethonium (1.5 mg/kg) are injected within 25 seconds, as part of a rapid sequence induction, there is no significant increase in IOP compared to baseline. This will now allow a more logical assessment of the total balance of risks to an inadequately starved patient with a penetrating eye injury.

Acknowledgments

We wish to acknowledge the secretarial help of P. Walls and L. Walton.

Appendix. Type II error

It is necessary before applying statistical tests to analyse experimental data to state the hypothesis these statistical methods will test. This hypothesis is usually that there is no difference between the groups studied and is called the null hypothesis.

There are four possible outcomes of the statistical tests. Ideally they will either accept the null hypothesis when it is true, or reject the null hypothesis when it is false. However, there are two further outcomes which will result in false judgements. First, the results may reject the null hypothesis when in fact it is true. This is known as the type I error and has a probability α. Second, the results may accept the null hypothesis when in fact it was false. This is known as the type II error and has a probability β. Awareness of both errors is essential if the results are not to be misleading.

The type I error is simple to identify and a level of 5% is commonly taken as standard, that is $p = 0.05$. This level of probability is easily assessed by reference to tables of critical values.

Type II errors, however, are more complex and not so easily assessed. The null hypothesis in this paper was accepted in Group A. The risk of obtaining this result when the opposite is true must therefore be assessed. The risk cannot be assessed by reference to tables and will vary with: the number in the study; the level of probability at which the difference between the means become significant; and the ratio of the difference betweeen the means with the standard deviation.

Increasing the values of these three variables will decrease the type II error, that is increasing the number in the study from 15 to 100 will substantially reduce the type II error. Graphs can be constructed which combine these factors and the graph used to assess the type II error for Group A

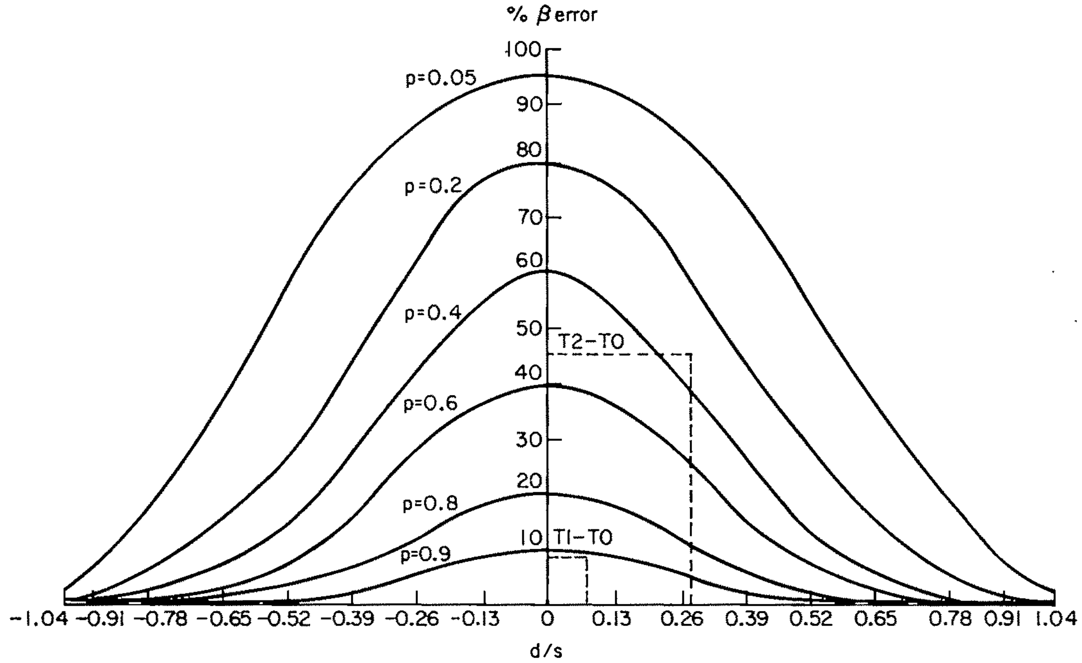

Fig. 1a. Type II (β) error graph when $n = 15$. For p value, d/s, see footnote to Table 2a.

Table 2a. The type II error in Group A.

	T1–T0	T2–T0	T3–T0	T4–T0	T5–T0
% error	9	45	30	43	55
p	0.93	0.29	0.70	0.48	0.35
d/s	0.07	0.29	0.09	0.18	− 0.24

p, probability value at which the difference between the means were significant, that is the maximum level of significance at which the null hypothesis can be accepted.
d, numerical difference between the means.
s, standard deviation.

is illustrated (Fig. 1a). Table 2a gives the probability values at which the difference between the means were significant and the ratio of difference between the means to standard deviation, for Group A. From these values the type II errors can be assessed by reference to the graph. The results for T1–T0 and T2–T0 are illustrated on the graph. Values greater than 50% would put in doubt the acceptance of the null hypothesis. Therefore, the type II errors for T1–T0, T2–T0, T3–T0, T4–T0, are acceptable; but for T5–T0 there is a 55% chance that the decrease in IOP was a significant fall.

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Prophylaxis against acid aspiration syndrome

Single oral dose of H_2-antagonist on the evening before elective surgery

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Summary

We have compared famotidine 40 mg, ranitidine 300 mg and placebo given in a single oral dose at 2200 hours as the sole means of prophylaxis in 286 patients who underwent elective surgery the following day. Standardised premedication was administered and anaesthesia induced. Gastric contents were aspirated by nasogastric suction and the pH and volume measured. Median values of pH after famotidine, ranitidine and placebo were 6.17, 6.74 and 2.45 respectively; median aspirate volumes were 8, 8 and 10 ml respectively. The proportions of patients considered 'not at risk' (pH >2.5) were 90% after famotidine, 91% after ranitidine and 52% after placebo. We conclude that the administration of a potent H_2-antagonist in a single oral dose at night offers a convenient routine means of providing extensive prophylactic cover in patients scheduled to undergo elective surgery the following day.

Key words

Complications; aspiration.
Histamine; ranitidine, famotidine.

The syndrome of respiratory distress, cyanosis and tachycardia after the aspiration of acidic gastric contents, first described by Hall in 1940,[1] is still responsible for 25% of all maternal anaesthetic deaths.[2] The risk of acid aspiration syndrome is not confined to obstetric patients; most patients prepared for elective surgery have highly acidic gastric contents[3,4] and may be subject to regurgitation.

Attempts to provide effective prophylaxis have centred on methods that increase the pH of gastric contents because the severity of pneumonitis is related to the degree of acidity of the aspirated fluid. Antacids are effective in raising gastric pH above 2.5 in most patients but there are problems associated with their use. They are short-acting, increase the volume of gastric contents, may not mix adequately with gastric fluid and can cause nausea and diarrhoea.[5,6] Particulate antacids may cause pneumonitis if aspirated.[7]

The introduction of the H_2-receptor antagonists has allowed elevation of intragastric pH by inhibition of gastric acid secretion. Cimetidine has been examined as a prophylactic agent in various doses, routes of administration and intervals before surgery.[8–13] Ranitidine has been favoured recently because of its greater potency, longer duration of action and absence of effects on hepatic drug metabolism.[3,4,14–16] Both drugs have proved to be most effective in raising gastric pH when two doses have been used, the first administered on the evening before surgery and the second on the following morning.[4,11,14] To date, however, single dose studies have examined administration only on the day of surgery, usually with premedication.

Famotidine is a new H_2-receptor antagonist, which is more potent than ranitidine but with a similar duration of action.[17] Famotidine does not interfere with the hepatic metabolism of drugs and has no known drug interactions. Famotidine and ranitidine administered in the evening reduce gastric acidity substantially for approximately 12 hours in nonfasted volunteers.[18] Gastric acid secretion in fasted subjects has been shown to exhibit a circadian rhythm with highest acid output during the night.[19] We therefore postulated that inhibition of this nocturnal secretion with an evening dose of an H_2-antagonist in patients fasted for surgery would increase gastric pH during the following morning in the absence of meal-stimulated acid output.

Methods

Three hundred patients aged 18–60 years who presented for elective surgery were recruited into the study. Patients were excluded if they were to undergo ophthalmic or upper gastrointestinal surgery, or had a history of upper gastrointestinal surgery. Those with significant cardiac, respira-

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Table 1. Patient details.

	Famotidine	Ranitidine	Placebo
Patients (*n*)	114	116	56
Sex (% female)	32	40	43
Smoking (% smoking)	33	32	43
Age, years; mean (SD)	34.7 (10.6)	34.9 (15.7)	34.9 (12.6)
Weight, kg; mean (SD)	69.8 (9.4)	70.4 (11.0)	69.2 (10.2)
* Interval, hours; mean (SD)	12.98 (2.52)	12.89 (2.43)	13.45 (2.56)

* Interval between drug administration and gastric aspiration.

Table 2. pH and volume of gastric aspirates after induction of anaesthesia in patients who received famotidine 40 mg, ranitidine 300 mg or placebo on the evening before surgery.

	Famotidine	Ranitidine	Placebo
pH, median (range)	6.17* (1.48–8.18)	6.74* (1.31–8.20)	2.45* (1.29–8.14)
Volume, ml; median (range)	8† (0–50)	8† (0–65)	10† (0–210)
Bile contamination, *n* (%)	31 (27)	27 (23)	13 (23)

* Active as compared with placebo, $p < 0.01$; famotidine as compared with ranitidine, NS.
† Active as compared with placebo, NS.

Table 3. Numbers and proportions of patients 'not at risk'.

	Famotidine	Ranitidine	Placebo
$pH > 2.5$	103 (90%)*	106 (91%)*	29 (52%)*
$pH > 3.5$	97 (85%)*	99 (85%)*	22 (39%)*
Volume < 0.4 ml/kg	101 (89%)†	106 (91%)†	47 (84%)†

* Active as compared with placebo, $p < 0.001$; famotidine as compared with ranitidine, NS.
† Active as compared with placebo, NS.

tory, renal or hepatic disease, allergy (including sensitivity to H_2-antagonists), or haematological abnormality were not included. Informed consent was obtained from all patients and the study was approved by the ethics committee of the James Connolly Memorial Hospital.

Patients were allocated by means of a randomised schedule to one of three groups, in proportions of 2:2:1; group 1 received famotidine 40 mg, group 2 ranitidine 300 mg and group 3 placebo. Blindness was maintained by using the 'double-dummy' technique. In each case the study medication was administered as a single dose at 2200 hours on the evening before surgery. Premedication was standardised to intramuscular atropine 0.6 mg and papaveretum 15–20 mg one hour before surgery; induction of anaesthesia comprised intravenous thiopentone 3–4.5 mg/kg and suxamethonium 1 mg/kg was administered to facilitate tracheal intubation.

A 16–18-gauge salem nasogastric tube was introduced into the stomach after tracheal intubation and complete removal of the gastric contents was attempted by repeated aspirations with a 60-ml syringe. The time of aspiration was noted and the aspirate examined visually for evidence of bile contamination. The total volume was then recorded and the pH measured using a Philips PW 9421 pH meter, which was calibrated daily with buffer solutions of pH 4 and 7.

Values of pH are not distributed normally;[20] consequently, the nonparametric Wilcoxon Rank Sum test was used to test for significance of pH distribution between active treatment and placebo, and between the two active treatment groups. Patients were defined as 'at risk' if their aspirate pH value was below or equal to 2.5; a more stringent pH level of 3.5 was also examined. Aspirate volumes above 0.4 ml/kg body weight were also considered as a secondary risk factor. Proportions of patients 'at risk' and 'not at risk' were compared using the Chi-squared test. We recognise that potential inaccuracy exists in the estimation of aspirate volumes, and so these data were grouped and also analysed by Chi-squared test.

Results

Fourteen patients did not complete the study through cancellation of surgery, and data from 286 patients were available for analysis. The three groups were well matched in respect of age, sex and weight distribution. The incidences of smoking in the 24 hours before the study period, and mean intervals between drug administration and sampling of gastric contents were similar among the groups (Table 1).

pH values of gastric aspirate were significantly higher in both active treatment groups compared with the placebo group ($p < 0.01$). There was no significant difference between the famotidine and ranitidine groups (Table 2). A trend towards lower aspirate volumes in the active treatment groups did not reach significance. The numbers of samples in the three groups with evidence of bile contamination are also shown in Table 2. Table 3 shows the numbers and proportions of patients considered 'not at risk' at induction of anaesthesia.

Intragastric pH values, plotted against the interval between drug administration and aspiration before surgery, are shown for each of the three groups in Figure 1. Figure 2 is a cumulative distribution graph that shows percentages of readings above specified pH values. Side effects reported during the study were few and mild. Five patients in the ranitidine group complained of nausea and/or flatulence, or a sense of fullness. Nausea, headache or sweating were reported by three patients in the famotidine group. Dry

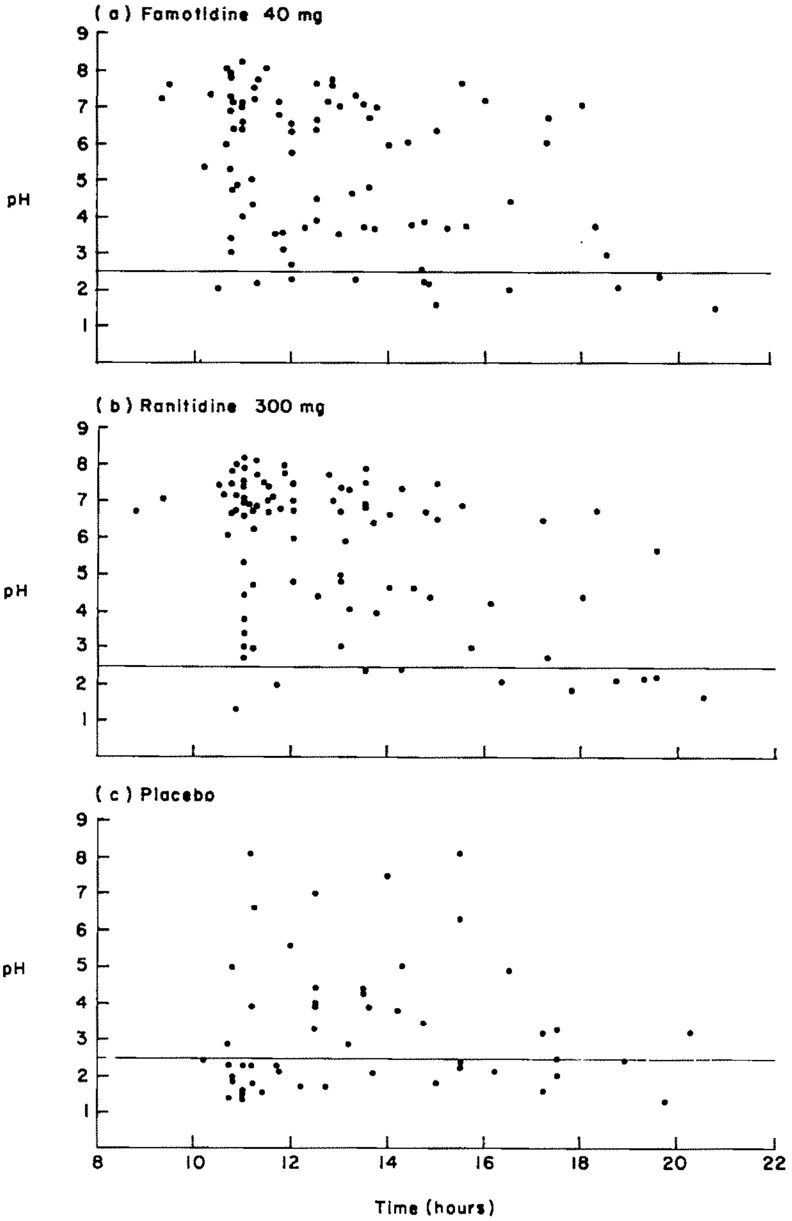

Fig. 1. Distribution of gastric aspirate pH values plotted against the interval between drug administration and gastric aspiration. Horizontal line represents 'safe' pH. (a) Famotidine 40 mg; (b) ranitidine 300 mg; (c) placebo.

mouth and nausea, and heartburn were reported by two patients in the placebo group.

Discussion

This study demonstrates that a single oral dose of a potent H_2-antagonist administered on the evening before surgery increases the pH of gastric contents in most elective surgical patients to 'safe' levels at the time of tracheal intubation. Effective ($pH > 2.5$) prophylaxis rates of around 90% compare well with results obtained from multiple dose studies; one study reported values of up to 100% but this involved a small number of patients.[4] The high proportion of pH values above 2.5 in the two active treatment groups supports our hypothesis. The absence of daytime meal-stimulated acid secretion and suppression of nocturnal acidity results in very few patients with a highly acidic gastric residue before surgery. The graphs of individual pH values plotted against the interval between drug administration and gastric aspiration indicate that the few prophylactic failures ($pH < 2.5$) occurred throughout the range of intervals. This suggests that the length of time after drug administration may not have been the sole, or even the most important, factor that influenced gastric pH. A number of individuals may for some reason be less responsive to H_2-receptor blockade, or have higher than average fasting acid output.

The duration of action of famotidine has been reported as approximately 30% longer than those of cimetidine or ranitidine when equipotent doses are used.[21] However, 24-hour intragastric acidity monitoring in nonfasted volunteers indicates that both famotidine 40 mg and ranitidine 300 mg cause profound inhibition of night-time acid secretion with little or no effect on acid output on the next

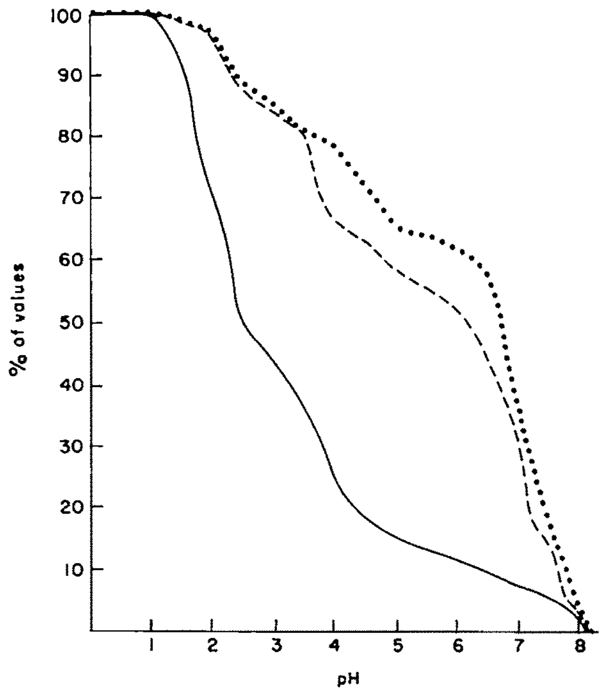

Fig. 2. Cumulative frequency distribution showing proportions of gastric aspirate values above specified pH values: famotidine 40 mg (---); ranitidine 300 mg (···); placebo (——).

day.[18] Our results in fasted patients did not reveal any observable difference in the duration of action of these two agents.

In this study 52% of the placebo group were found to have an aspirate pH above 2.5. Andrews *et al.*[4] also used atropine premedication, and found that 68% of placebo-treated patients had a gastric pH that exceeded 2.5. These findings contrast with studies in which no anticholinergic premedication was used; 25% or less of placebo-treated patients had a gastric pH above 2.5.[3,9,15] This suggests that anticholinergic premedication has some effect in elevation of gastric pH, and is probably responsible also for the relatively low distribution of aspirate volumes in the placebo group.

Distributions of gastric aspirate volumes in both treatment groups were similar and lower than in the placebo group, although significance was not reached. Mendelson[22] proposed originally that a volume of gastric contents of more than 25 ml was an additional risk factor in combination with low pH. The method used for aspiration in this study cannot be guaranteed to provide complete emptying of the stomach, and values have been regarded as approximations. In addition, duodenogastric reflux was present in 20–30% of all patients; this increases the volume of gastric contents and could be a confounding factor in comparisons between groups, particularly when using threshold values. We have taken gastric pH as the principal risk factor for these reasons, in common with other investigators. Adverse events that may have been attributable to treatment were few and without exception mild, in keeping with the findings of other studies on pre-operative use of H_2-antagonists.

In conclusion, potent H_2-antagonists administered as a single oral dose on the evening before surgery appear to offer a simple routine method for extensive prophylactic cover in patients scheduled to undergo elective surgery. Use of the intravenous route will continue to be necessary before emergency surgery or in patients unable to tolerate oral administration.

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Continuous blockade of the lumbar plexus after knee surgery—postoperative analgesia and bupivacaine plasma concentrations

A controlled clinical trial

J. B. DAHL, C. L. CHRISTIANSEN, J. J. DAUGAARD, P. SCHULTZ AND P. CARLSSON

Summary

In a double blind, randomised, controlled investigation the analgesic effect of a continuous block of the lumbar plexus with bupivacaine compared with sodium chloride was examined in 20 patients with postoperative pain after knee-joint surgery. The infusion was given through a catheter inserted in the neurovascular fascial sheath of the femoral nerve, according to the three-in-one block technique. The patients treated with bupivacaine had significantly lower pain scores and a significantly lower demand for morphine. Side effects related to the catheters or the infusions of bupivacaine were not observed.

Key words

Anaesthetic techniques, regional; lumbar plexus.
Anaesthetics, local; bupivacaine.

Blockade of the lumbar plexus by the inguinal paravascular technique (three-in-one block) was described by Winnie in 1973.[1] The femoral, the lateral cutaneous femoral, and the obturator nerves are blocked by this method, which results in analgesia of major parts of the lower extremity. The introduction of a catheter in the fascial sheath of the femoral nerve permits a continuous block of the lumbar plexus.[2,3] The clinical application of this method is, however, not yet evident and only a few controlled investigations have attempted to elucidate this.

The use of the three-in-one block in uncontrolled studies and case reports is claimed to relieve pain after surgery on both the femoral neck[3,4] and the knee joint.[2] Patel *et al.*[5] in a controlled investigation found the method suitable for arthroscopy of the knee in day clinic patients. The purposes of this investigation were to evaluate the analgesic effect of a continuous block of the lumbar plexus after knee-joint surgery and to measure the venous plasma concentrations of bupivacaine during the treatment.

Methods

Twenty patients undergoing elective open knee-joint surgery participated. All gave their informed consent in accordance with the Helsinki II declaration, and the investigation was approved by the regional Ethics Committee and the Danish National Health Service.

Premedication consisted of diazepam 0.25 mg/kg given orally. Anaesthesia was induced with thiopentone and pethidine given intravenously and maintained with enflurane, nitrous oxide and pethidine when needed. Tracheal intubation was facilitated by atracurium and ventilation controlled. Residual neuromuscular block was reversed with neostigmine and atropine at the end of the operation. A catheter (Portex, epidural, 16-G) was placed in the fascial sheath according to the technique described elsewhere after surgery but before the patients were awake.[6] The catheter was advanced 15–20 cm cranially.

The patients were selected randomly into two groups to be treated with the same volume of either bupivacaine or isotonic sodium chloride through the catheter. A bolus dose, 2 mg/kg bodyweight, of bupivacaine 5 mg/ml was injected in the patients treated with bupivacaine immediately after the catheter insertion. This was followed by a constant infusion of bupivacaine 2.5 mg/ml, 0.35 mg/kg/hour. Isotonic sodium chloride was given to the control group as a bolus dose, 0.4 ml/kg, followed by a constant infusion of sodium chloride 0.14 ml/kg/hour; blinded syringes and infusion sets were used. The patients were unaware of the nature of the block and the infusion was maintained for 16 hours. All patients also received suppositories with acetylsalicylic acid, 1.5 g every 6 hours.

Patients received morphine 2.5 mg intravenously on demand during the first 2 hours after operation and over the next 14 hours morphine 0.125 mg/kg was given intramuscularly on demand. This treatment was administered by

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recovery ward nursing staff, experienced in postoperative pain treatment, who were unaware of the nature of the block. The demand of morphine was registered.

Pain intensity was recorded on a visual analogue scale (VAS) (0–100 mm: 0 mm, no pain; 100 mm, worst pain imaginable) 2, 4, 6, 8, 12 and 16 hours after operation. The occurrence and severity of nausea was recorded 16 hours postoperatively using a verbal scale (none, light, moderate, pronounced) and the presence of vomiting was noted. The need for catheterisation of the bladder was also noted and if more than 500 ml of urine were evacuated, the patients were said to have urinary retention. The patients were asked to record, on a verbal scale, their satisfaction with the pain treatment (most satisfactory, satisfactory, less satisfactory, not satisfactory) at the end of the infusion period.

Cutaneous sensation (pinprick) in the areas innervated by the femoral and the cutaneous femoral lateral nerves of all the patients was examined. Bandages prevented examination of the area innervated by the obturator nerve on the medial side of the knee joint. Venous blood samples were taken from all the patients 0.5, 1, 4 and 16 hours after the start of the infusion, to determine the plasma concentration of bupivacaine by gas chromatography. Only the blood samples from patients who had been treated with bupivacaine were analysed.

The data are described by median values and ranges. Statistical analyses were performed with the Mann–Whitney test and Friedman's two-way analyses of variance; significance, $p < 0.05$.

Results

Patient data, duration of surgery and peroperative consumption of pethidine are shown in Table 1. Hypaesthesia was found in the area innervated by the femoral nerve in all 10 patients treated with bupivacaine, and in eight patients in the area innervated by the cutaneous femoral lateral nerve. Hypaesthesia was not present, however, in those patients treated with sodium chloride.

A significant difference was found between the groups in both the supplementary consumption of morphine and the pain intensity evaluated on the VAS (Table 2, Fig. 1). Visual analogue scores are compared as median values of the scores of each patient from the second to the sixteenth hour. Friedman's two-way variance analyses showed that on the whole, pain intensity in the groups lessened in time, but it did not show statistically significant interaction between time and treatment.[7]

Table 2 lists the morphine consumption in the two treatment groups. Seven patients treated with bupivacaine needed less than morphine 10 mg, while one needed a total of morphine 49 mg and had an average pain score of 59 mm. This occurred despite the presence of hypaesthesia in the areas innervated by the femoral and the cutaneous femoral lateral nerves, which was taken as a sign of the correct position of the catheter. There was no significant difference between the groups with regard to postoperative nausea, vomiting or urinary retention (Table 3). The patients treated with bupivacaine were significantly more satisfied with the treatment (Table 4). Bupivacaine concentrations in venous blood are shown in Figure 2. Symptoms of toxic reactions were not observed. The catheters were removed at a median of 72 hours (range 24–144 hours) after the operation. We found no signs of infection at the insertion site and none of the patients complained of inconvenience from the catheter.

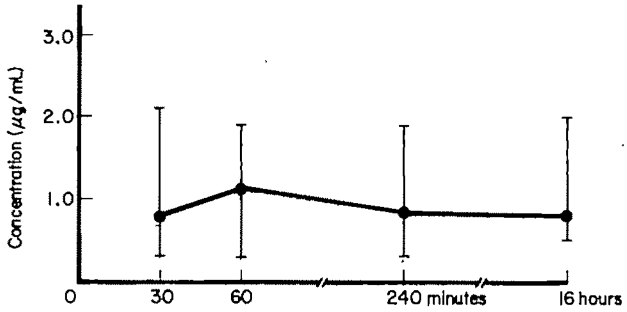

Fig. 1. Median VAS-scores during the first 16 postoperative hours in the two treatment groups, ○, bupivacaine treated; ●, sodium chloride treated. $p < 0.01$ (Mann–Whitney *U* test).

Table 1. Demographic data of patients with median values and ranges. No significant differences ($p > 0.05$) were found (Mann–Whitney *U* test).

	Bupivacaine group	Sodium chloride group
Sex (M/F)	3/7	2/8
Age, years	21 (17–34)	22 (20–42)
Height, cm	171 (165–192)	167 (150–183)
Weight, kg	65 (50–87)	60 (52–96)
Duration of surgery, minutes	100 (25–180)	120 (60–225)
Peroperative pethidine, mg	105 (70–155)	100 (50–125)

Table 2. Postoperative demand (during 16 hours) for morphine in the two treatment groups. $p < 0.01$ (Mann–Whitney *U* test).

	Bupivacaine group (*n*)	Sodium chloride group (*n*)
0 mg morphine	4	0
2.5–20 mg morphine	4	1
21–40 mg morphine	1	5
41–60 mg morphine	1	4

Table 3. Side effects. $p > 0.05$ (Mann–Whitney *U* test).

	Bupivacaine group ($n = 10$)	Sodium chloride group ($n = 10$)
Nausea		
None	6	5
Light	3	0
Moderate	1	3
Severe	0	2
Patients who vomited	2	5
Patients who needed catheterisation of the bladder	2	5

Table 4. Patient acceptance of treatment, $p < 0.01$ (Mann–Whitney *U* test).

	Bupivacaine group	Sodium chloride group
Most satisfactory	8	0
Satisfactory	1	6
Less satisfactory	1	2
Not satisfactory	0	2

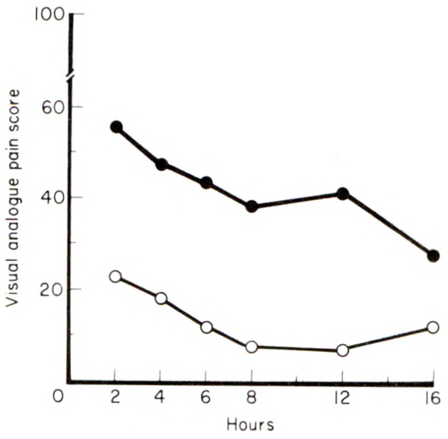

Fig. 2. Median plasma bupivacaine concentration (+ range) in 10 patients treated with perifemoral infusions of 0.25% bupivacaine after knee joint surgery.

Discussion

Postoperative pain after explorative knee surgery is often pronounced and the conventional methods of treatment are all associated with various side effects. It has been shown in controlled investigations that epidural morphine gives superior pain relief compared to conventional intramuscular treatment with opioids.[8] However, side effects such as nausea, vomiting, urinary retention, pruritus and respiratory depression indicate that epidural morphine is not the optimal treatment.[9] Local anaesthetics administered epidurally may cause hypotension and the bilateral motor block is inappropriate in the postoperative period. Continuous block of peripheral nerves compared with the analgesia above has theoretical advantages since it is local to the pain-causing extremity and thus the cardiovascular and respiratory effects are minimal.

The knee joint is innervated primarily by the femoral nerve. Furthermore the obturator nerve and branches of the sciatic nerve have a certain sensory function. Earlier investigations have shown good effects from an isolated block of the femoral nerve after knee surgery[10–12] and combined local blocks have been used both in adults[13] and children.[14] The clinical usefulness of these blocks has, however, been limited by the duration of action of the local anaesthetic agents used,[12] since a continuous technique has been described only in one case.[2]

The blinding of such an investigation must be incomplete as a result of cutaneous hypaesthesia and paralyses in the patients treated with bupivacaine. However, the double blinded principle was maintained as far as possible in this study. The continuous block of the lumbar plexus after surgery to the knee was found to be good and reliable. Both morphine consumption and pain intensity were reduced in comparison with the placebo group, and the patients treated with bupivacaine were very satisfied with this form of pain treatment. The patient mentioned above (who needed morphine 49 mg) had had the same knee operated on three times and each time experienced severe postoperative pain. She was less satisfied with the current treatment.

It is to be anticipated that side effects related to opioids will be less frequent after a three-in-one block with bupivacaine, but the number of patients in this study was too small to permit conclusive statistical evidence. Blockade of the lumbar plexus started before surgery could possibly further reduce the demand for opioid per- and postoperatively.[10]

No patient exhibited signs of toxicity related to the use of bupivacaine. The median venous plasma concentrations never exceeded 1.2 μg/ml and the maximal peak measured was 2.1 μg/ml (in one patient after 30 minutes) (Fig. 2). Tucker[15] in a recent review referred to estimates of threshold plasma concentrations of various local anaesthetics associated with the onset of central nervous system toxicity in man. These ranged from 2–4 μg/ml for bupivacaine. A review by Reynolds[16] indicates that mild toxicity may occur at plasma concentrations of 1.6–2 μg/ml, with risks of serious toxicity at 2.3–5 μg/ml.

The catheters did not cause any inconvenience and no signs of infection were observed; the method is simple and does not demand special positioning of the patient. However complications of this method have been described in one case: an acute compression syndrome of the femoral nerve caused by a subfascial haematoma.[17] All the catheters in the bupivacaine group were placed correctly when judged by the pinprick test in the cutaneous areas of innervation. A nerve stimulator is not necessary. Winnie *et al.*[1] used the causation of paraesthesiae to locate the nerve and a method based on 'loss of resistance' has also been described.[18] No controlled investigations have shown that the use of a nerve stimulator increases the rate of success or causes fewer neuropathies, but we consider that it may be a valuable tool when inserting catheters in anaesthetised patients.

In conclusion, this study demonstrates that continuous blockade of the lumbar plexus with bupivacaine through a catheter placed in the sheath of the femoral nerve is a safe and reliable technique. It significantly reduces postoperative pain and the need for opioids in the postoperative period after knee-joint surgery.

Acknowledgments

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Anaesthesia, 1988, Volume 43, pages 1019–1021

Alkalinised bupivacaine and adrenaline for epidural Caesarean section

A comparison with 0.5% bupivacaine

R. M. TACKLEY AND A. J. COE

Summary

Twenty-four mothers received either 0.5% bupivacaine (group 1, n = 14), or alkalinised 0.5% bupivacaine and 1 in 200 000 adrenaline (group 2, n = 10), as an epidural local anaesthetic for elective lower segment Caesarean section in a randomised, double blind study. The two groups were prepared for surgery according to an identical technique. Onset of analgesia to pinprick was significantly faster in group 2 (p < 0.02). Group 1 required additional analgesia during surgery significantly more often than those in group 2 (p = 0.04). Significantly more patients in group 2 were ready for surgery by the time limit for the study (45 minutes, p = 0.002). Onset of motor blockade was significantly faster in group 2 (p = 0.01). There were no significant differences between the two groups with regard to duration of surgery, or Apgar scores at 1 and 5 minutes. Alkalinised 0.5% bupivacaine and adrenaline was superior to 0.5% bupivacaine for epidural Caesarean section.

Key words

Anaesthetic techniques, regional; epidural.
Anaesthetics, local; bupivacaine.

The benefits of adding adrenaline to bupivacaine are disputed. Increased duration of action has been shown in labour,[1,2] for elective Caesarean section[3] and in general surgery,[4] but other workers have not found this in labour[5] or for elective Caesarean section.[6] Plasma bupivacaine levels are reduced when adrenaline is used with bupivacaine in labour,[5,7] and this advantage has also been demonstrated in patients who undergo elective Caesarean section.[3,6] Adrenaline is both unstable and insoluble in alkaline solution[8] and commercially produced bupivacaine with 1 in 200 000 adrenaline has a low pH (approximately 3.8).[9] A slow onset of action should be expected with such a solution and this has been confirmed for epidural anaesthesia in the nonpregnant[4] and during epidural anaesthesia for elective Caesarean section.[3]

pH modified bupivacaine with 1 in 200 000 adrenaline might be expected to display the advantages of adrenaline addition without its slow onset. The purpose of this study was to compare alkalinised, commercially available 0.5% bupivacaine with 1 to 200 000 adrenaline, with 0.5% bupivacaine plain as epidural local anaesthetics for elective Caesarean section.

Method

pH studies

Bupivacaine 0.5% plain (Marcain steripack) and 0.5% bupivacaine with 1 in 200 000 adrenaline (Marcain steripack) were used for this study. The pH of four 10-ml samples from each of the local anaesthetic batches to be used was measured before clinical work began. Aliquots of 8.4% preservative-free sodium bicarbonate solution were added to the bupivacaine and adrenaline ampoules and the pH was measured after each addition. The presence of a temporary or permanent precipitate was also recorded. All pH measurements were made at 21°C using a Griffin digital pH meter, regularly calibrated with British Drug Houses buffer solution pH 4 and 7.

Clinical study

Written, informed consent was obtained from 25 ASA grade 1 and 2 mothers listed for elective lower segment Caesarean section under epidural anaesthesia, after approval from the local ethics committee. They were allocated randomly to one of two groups: group 1 received 0.5% plain bupivacaine and group 2 bupivacaine 0.5% with 1 in 200 000 adrenaline to which 0.15 ml of 8.4% preservative-free sodium bicarbonate had been added to each 10 ml ampoule. Two investigators carried out the work. The first drew up the allocated solution into syringes labelled Marcain only. He then handed the solution to the second investigator, who, along with the mother remained unaware of the contents for the entire procedure. The second investigator cannulated the epidural space at the L_{2-3} or L_{3-4} level, and inserted 3.5 cm of catheter. The circulation of

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the parturients was preloaded with one litre of compound sodium lactate solution, and measurements of pulse rate and arterial blood pressure were taken at frequent intervals throughout the study. The fetal heart rate was also checked at intervals.

A test dose of 4 ml of the chosen solution was given in the sitting position. From this time until completion of the study the level of any sensory block to pinprick and the degree of motor block in each leg (0, normal power of hip flexion; 1, reduced power; 2, no power) were measured and recorded every 5 minutes by the second investigator. The first investigator remained in the room for optimum patient safety. Five minutes later, 10 ml of the chosen solution was given in the sitting position, and this was taken as time 0 for the study. Intravenous ephedrine and compound sodium lactate solution were given as necessary throughout the procedure to maintain the arterial pressure. The mothers' position was changed to left lateral at 10 minutes.

A further dose of the same local anaesthetic was given at 20 minutes if the block to pinprick had not reached T_7. For levels T_{10} or lower, mothers received 10 ml, for T_{9-7}, 5 ml. Observations were continued until an ascending, bilateral pinprick block to T_7 was achieved, when the mother was taken into the operating theatre for surgery to commence. The investigators were allowed to take any steps required to achieve this level as rapidly as possible, using the chosen solutions, if it had not been reached by 45 minutes. The need for intra-operative supplementary analgesia was recorded as was the Apgar score of the neonate at 1 and 5 minutes. The duration of surgery and grade of the surgeon were recorded.

Results

pH measurements

Table 1 shows the results of the pH measurements. Twelve ampoules were tested and the critical pHs were in agreement with manufacturer's specification. At least 0.25 ml of sodium bicarbonate solution had to be added before permanent precipitation occurred.

Table 1. pH measurements of the local anaesthetic solutions used.

Plain 0.5% bupivacaine 10 ml (Marcain steripack)

Batch no.	pH
427	4.9
427	5.1
427	5.3
427	5.1
433	5.1
433	5.1
433	5.2
433	5.4

Bupivacaine with 1 in 200 000 adrenaline 10 ml (Marcain steripack)

		pH + sodium bicarbonate			
Batch no.	pH	0.05 ml	0.15 ml	0.25 ml	0.4 ml
518	3.44	6.0	6.3pr	6.8pp	7.1pp
518	3.7	6.2	6.4pr	6.7pr	7.2pp
518	3.3	6.0	6.4pr	6.6pr	7.0pp
518	3.3	6.1	6.3pr	6.6pr	7.2pp

pr, precipitate which redissolves; pp, permanent precipitate.

Table 2. Patient details.

	Group 1 (n = 14)	Group 2 (n = 10)
Height, m (SD)	1.57 (0.18)	1.57 (0.9)
Weight, kg (SD)	72 (13)	67 (13)
Duration of surgery, minutes (SD)	41 (11)	43 (4)
Apgar scores		
1 minute, median (range)	9 (7–9)	9 (6–9)
5 minutes, median (range)	10 (9–10)	10 (9–10)

Table 3. Results of clinical study.

	Group 1 (n = 14)	Group 2 (n = 10)
Time ready for theatre, minutes, median (range)	45 (25–90)	30 (20–45)
Time to onset of pinprick block, minutes, median (range)	10 (5–15)	5 (>5–10)
Number with motor block at 10 minutes	5	10
Number requiring peroperative supplements	7	0

Clinical study

Table 2 shows patient height, weight, the duration of surgery and Apgar scores for the two groups. There were no significant differences between the two groups with respect to these variables.

Table 3 shows the results of the clinical study. It was found that group 2 required additional peroperative analgesia significantly less often than those in group 1 (Fisher's exact probability test, $p = 0.04$). The peroperative supplements used were Entonox, intravenous opioids or additional epidural local anaesthetic. The patients in group 2 were also significantly more likely to be ready for surgery by the 45-minute time limit of the study (Fisher's exact probability test, $p = 0.002$). The onset of pinprick block was significantly faster in group 2 (Chi-squared test with Yates' correction, $p = 0.01$–0.02). Onset of motor blockade was significantly faster in group 2 (Fisher's exact probability test, $p = 0.01$). One mother's results were omitted because of failure to keep to protocol.

Discussion

This study suggests that pH modified 0.5% bupivacaine and 1 in 200 000 adrenaline is more likely to produce adequate anaesthesia for elective Caesarean section in a given time than 0.5% plain bupivacaine. A more rapid onset of both sensory and motor blockade was also shown, which emphasises the real difference between the solutions used. We found, as have other workers,[3,6] that the reduced requirement for analgesic supplementation peroperatively suggests that bupivacaine with adrenaline may produce a more reliable and effective blockade. The disadvantage of using bupivacaine and adrenaline alone appears to be a slower onset of action.[3] This can result in the parturient having to endure up to 90 minutes in the anaesthetic room before her operation, although this time may be reduced when single-dose techniques are used.[10]

The pKa of plain bupivacaine is 8.1, while the pH is only 4–5.5.[11] To guarantee the stability of the adrenaline, commercial bupivacaine 0.5% with adrenaline mixtures are acidified to pH 3.3–3.8. There is less bupivacaine in the unionised form at this lower pH and this may explain a slower onset of action. An improvement in the rate of onset by raising the pH 1 or 2 units has been shown for plain bupivacaine,[12,13] and also suggested for bupivacaine plus adrenaline mixtures.[9,13] This solution is stable for up to 6 hours after mixing,[14] and has already been shown to reduce onset time and prolong brachial plexus blockade,[9] whilst pH modification alone failed to do this.[15]

We confirmed in our initial pH studies that 0.15 mmol sodium bicarbonate will raise the pH by up to 3 units to give a final pH of around 6.5. Accurate measurements of such small volume was difficult; a large safety margin was left below the 0.25 ml volume which could cause permanent precipitation of the mixture. Thus only 0.15 ml of bicarbonate was added to each 10 ml of solution.

In summary, the theoretical advantages of pH-modified 0.5% bupivacaine and adrenaline over 0.5% bupivacaine for elective epidural Caesarean section have been supported by this clinical trial.

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Anaesthesia, 1988, Volume 43, pages 1022–1023

CASE REPORT

Is propofol a safe agent in porphyria?

P. M. WEIR AND B. P. HODKINSON

Summary

A case is presented of the use of a propofol infusion for anaesthesia in a patient with known variegate porphyria. Urinary screening for porphyrins demonstrated a marked increase after this anaesthetic, but there were no clinical symptoms.

Key words

Anaesthetics, intravenous; propofol.
Complicaitons; porphyria.

The term porphyria describes a group of disturbances in porphyrin metabolism characterised by a marked increase in the formation of porphyrins and, or, precursors. This results in the tissue accumulation of these compounds with increased urinary and faecal excretion. Acute hepatic porphyrias are of greatest importance to the anaesthetist. These include acute intermittent porphyria, variegate porphyria and hereditary coproporphyria. An acute attack in these patients may be precipitated by various anaesthetic drugs. The best known example is with the barbiturates thiopentone and methohexitone, but problems have also been reported with Althesin,[1,2] diazepam, etomidate infusion[3] and ketamine.[4] There have been reports recently that propofol[5,6] may be a safe agent to use in porphyria, but unfortunately in one study propofol was used only in a low dose for a very short procedure.[5]

We decided on the basis of these reports to give a patient known to have variegate porphyria a general anaesthetic with a propofol infusion.

Case history

A 35-year-old 75 kg male of South African descent was admitted after a fall from 5 metres in which he sustained severe bilateral forearm fractures. He had been diagnosed as having variegate porphyria one year before this. The diagnosis was made during screening of his family after a sister had developed an acute attack following an elective cholecystectomy. He had never had any clinical symptoms of the disease. Prior to this operation he had already had two anaesthetics during this admission, one for application of external fixators to both forearms and another the next day for release of acute carpal tunnel syndrome. The first anaesthetic was a balanced general anaesthetic that used propofol, nitrous oxide, oxygen, isoflurane, vecuronium and fentanyl. He received a supraclavicular brachial plexus block using 1.5% prilocaine for the carpal tunnel release. His urine screen for porphyrins after these operations was normal and he remained well with no clinical symptoms of the disease.

On this occasion, the third operative procedure in 3 days, the patient required open reduction and internal fixation of his left forearm. He gave unreserved consent after discussion of the type of anaesthetic to be used and possible effects with regard to his particular condition.

A urine sample was obtained for porphyrin screen immediately pre-operatively and a 24-hour collection started from the time of surgery. Anaesthetic induction was with propofol 200 mg, morphine sulphate 10 mg, and relaxation for tracheal intubation with suxamethonium 100 mg. The larynx was sprayed with 60 mg lignocaine. Anaesthesia was maintained with spontaneous breathing of nitrous oxide 50% and oxygen and a propofol infusion. The total dose of propofol for the 50-minute operation was 900 mg. Both the surgery and anaesthesia were uneventful; blood loss was minimal and the patient's cardiovascular system was stable throughout. Awakening was within minutes of the cessation of the propofol infusion. He complained of no symptoms associated with porphyria and remained well for the rest of his 2-week stay in hospital.

The results of the 24-hour urine collection after operation are given in Table 1. They show a marked elevation in porphobilinogen, uroporphyrin and coproporphyrin. Consultation with our biochemists revealed that the level of 26 μmol for porphobilinogen would normally be associated with clinical symptoms.

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Table 1. Results of urinary porphyrin analysis.

Pre-operative porphyrin screen	Normal
24-hour urine porphyrins	
Porphobinogen screen	Increased
Porphyrin screen	Increased
Porphobilinogen	26 μmol (normal 0–9)
Uroporphyrin	250 nmol (normal 0–36)
Coproporphyrin	1 553 nmol (normal 0–306)

Discussion

The exact mechanism of pathology associated with porphyria is not identified clearly. The most likely explanation is that it represents a breakdown in the control of haem formation. One theory is that the rate controlling enzyme is itself controlled by a repressor gene that in porphyria may be genetically abnormal or affected by various drugs. The symptoms of an acute attack are predominantly alimentary, cutaneous, neurological and cardiovascular. All may be caused by demyelination secondary to high levels of δ-aminolaevulinic acid synthase. Acute attacks of porphyria still carry a relatively high mortality and therefore the emphasis must be placed on prevention. Drugs known to precipitate acute attacks need to be avoided.

To determine whether a drug is porphyrinogenic most are tested on rat models, some of which are treated with 3,5-diethoxycarbonyl,1,4,dihydrocollidine to produce latent porphyria. Drugs which have been shown not to cause an increase in δ-aminolaevulinic acid synthase in these rats have been shown subsequently to cause an increase of porphyrins in humans, for example ketamine.[3,4] There are however many reports of the safe use of ketamine in porphyria.[7,8] This apparent contradiction may be because acute attacks of porphyria could be precipitated by other factors; for example, dehydration, surgical stress and nonanaesthetic drugs. Similarly not every administration of a known porphyrinogenic drug will precipitate an acute attack.[9] The patient in this case had a normal porphyrin screen on admission and again 48 hours later, after two surgical procedures. A screen for porphyrins was not made after his first anaesthetic using a propofol induction. There was no increase of urinary porphyrins associated with his initial trauma or surgery. None of the other agents used in his final surgical procedure has been shown to be porphyrinogenic. The very marked increases in porphobilinogen, uroporphyrin and coproporphyrin following the propofol infusion suggest strongly a causal relationship. On this basis we advise against the use of propofol in a patient with porphyria.

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Anaesthesia, 1988, Volume 43, pages 1024–1025

CASE REPORT

Delayed recovery from general anaesthesia

K. R. JOHNSTON AND R. S. VAUGHAN

Summary

A case of postoperative coma associated with diabetes insipidus and hypothermia is presented. Some recommendations are offered for the future management of similar cases.

Key words

Complications; hypothermia.
Recovery; delayed.

This is a report of a case of delayed recovery from general anaesthesia and of a possible clinical association not previously reported in the anaesthetic literature.

Case history

A 61-year-old miner was referred to the thoracic surgeons complaining of epigastric pain and dyspepsia. The symptoms were related to oesophagitis secondary to proven gastro-oesophageal reflux. The patient had a vagotomy and pyloroplasty several years previously for similar symptoms and this was followed by substantial relief. Epigastric pain and vomiting, aggravated by stooping and lying flat, had increased steadily particularly at night, during the year before this referral. These symptoms had been relieved initially by antacids and cimetidine.

He was investigated further in view of the progressive failure of medical management. Fibreoptic oesophagoscopy revealed severe oesophagitis and the barium meal was reported as showing a surgical deformity of the antrum and duodenal loop. He was being treated for hypertension with beta-adrenergic blockade, for oesophagitis with cimetidine and Gaviscon and for longstanding idiopathic diabetes insipidus with DDAVP (desamino-cysteine-d-arginine vasopressin) 1.5 ml twice daily nasally. Investigations, including pulmonary spirometry, were unremarkable. The patient consented to operation and was scheduled for left thoracotomy and fundoplication.

Anaesthetic technique

The patient received a premedication of intramuscular papaveretum 15 mg and hyoscine 0.3 mg 1.5 hours before induction of anaesthesia. A blood pressure cuff and ECG were applied and an intravenous infusion of compound sodium lactate solution was established. Pre-oxygenation for 3 minutes was followed by a rapid sequence intravenous induction using fentanyl 0.1 mg, thiopentone 250 mg and suxamethonium 100 mg. Cricoid pressure was applied as consciousness was lost and the patient was intubated with a 9.0 mm tracheal tube. Successful intubation was confirmed by auscultation. Anaesthesia was maintained with nitrous oxide, oxygen and enflurane. Pancuronium bromide (6.0 mg) was administered after the return of spontaneous muscle activity.

Fibreoptic bronchoscopy through the tracheal tube confirmed that the anatomy of the right bronchial tree was normal. Accordingly, cricoid pressure was re-applied, the tracheal tube removed and replaced by a large right-sided double lumen Robertshaw bronchial tube; correct placement of this tube was confirmed by alternate clamping and auscultation. The patient was positioned for a left thoracotomy. A thoracic epidural catheter was then introduced at the T_{5-6} interspace. Epidural fentanyl was used to produce analgesia after the technique described by Ahuja *et al.*[1] This involves giving 1.6 μg/kg in 10 ml saline as a loading dose followed by a constant infusion of fentanyl in saline at a dose of 0.5 μg/kg per hour.

Surgery started and an uneventful fundoplication was completed in 3.5 hours through a left thoraco-abdominal incision; about 85 minutes of one lung anaesthesia were required. Blood loss was estimated to be 500 ml: this was replaced with one litre compound sodium lactate and 500 ml polygeline, all infused at 37°C. Forty minutes after the start of surgery it was noted that the syringe containing the epidural infusion of fentanyl was half empty. Approximately 25 ml (containing 300 μg) fentanyl had been injected inadvertently; the pump was set at 30 ml/hour instead of the

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required 3.0 ml/hour. The infusion was stopped. The administration of enflurane was discontinued approximately 10–15 minutes before the end of surgery. The neuromuscular blockade was reversed with atropine 1.2 mg and neostigmine 2.5 mg and the patient's lungs ventilated with 100% oxygen. After a further 5 minutes, 7% carbon dioxide was added to the inspired gas but this produced no reaction.

We thought that the prolonged unconsciousness was related to the relative overdose of epidural fentanyl, but we considered it prudent not to attempt to reverse the respiratory depressant effect of the fentanyl with naloxone since this might also reverse its analgesic effect. Consequently cricoid pressure was re-applied, the double lumen bronchial tube was removed, replaced by a 9.0 mm tracheal tube and the patient transferred to the recovery room for elective ventilation and constant monitoring. The patient was unrousable on admission, unresponsive to painful stimuli and had small fixed pupils. Ventilation with 50% nitrous oxide in oxygen was continued. The arterial blood pressure remained at 130/90 mmHg but a bradycardia of 45 beats/minute had become established despite repeated doses of 0.3 mg intravenous atropine. Peripheral cyanosis began to develop despite the apparent adequate ventilation. A chest X ray was requested, the $F\text{IO}_2$ increased to 1.0 and a sample of arterial blood despatched for blood gases, electrolyte and glucose estimations. In addition 0.4 mg naloxone was administered intravenously along with a further 0.6 mg atropine; neither produced any effect.

The chest X ray, electrolytes and blood glucose were within normal limits and the blood gases report showed no abnormality except that the oxygen tension was high at 63 kPa. Four questions needed to be answered

> Why was the patient peripherally cyanosed despite a $P\text{aO}_2$ of 63 kPa?
>
> Why was the patient unconscious? If this was because of an overdose with fentanyl, why was there no response to naloxone?
>
> What was the cause of the atropine resistant bradycardia with a normal blood pressure?

The recovery nurse reported that she could not obtain a reading with a normal thermometer during the ensuing deliberations. A low reading thermometer was applied and an axillary temperature of below 32°C recorded. The patient was covered with a space blanket and a hot water humidifier added to the ventilator system. His temperature had increased to 34°C one hour later and this rise was accompanied by violent shivering. The temperature further increased to 35.5°C 25 minutes later, spontaneous breathing started, consciousness returned and the bradycardia disappeared.

A trial of 50% oxygen in air through a T-piece was started. The patient was extubated in the sitting position some 75 minutes later. The epidural fentanyl infusion was recommenced when the patient started to complain of pain and was continued for a further 72 hours. There were no further complications and the patient was discharged home after an uneventful recovery.

Three other patients had thoracotomies on the same day in the same theatre suite. The duration of surgery was comparable in all cases (range 2.5–3.5 hours). Measured blood loss was also comparable (300 ml) in two patients who required similar intravenous fluid replacement. The third patient had a measured blood loss of 1200 ml and required a three-unit blood transfusion and 1000 ml of compound sodium lactate solution. None of these patients had an axillary temperature recorded below 35°C on admission to the recovery room.

Discussion

It is our opinion that, contrary to our original impression, the relative overdose of epidural fentanyl was *not* responsible for the delayed recovery of our patient. We believe that the events and observations described were a direct result of central hypothermia secondary to subclinical pituitary dysfunction particularly since three other patients who had thoracotomies in the same theatre suite did not develop a similar degree of hypothermia.

Hypothermia is a well recognised complication of prolonged surgery particularly in the very young,[2,3] in the elderly[2,4] and when large body cavities are open to the atmosphere.[5] Patients with hypothyroidism[3] and myxoedema[2,3,6] are also recognised to be at increased risk of hypothermia after surgery.

Hypothalamic lesions are known to be associated with impaired thermoregulation[2,3,7] and such lesions can present as precocious puberty, hypogonadism, obesity or diabetes insipidus.[3] Indeed, unrecognised diabetes insipidus can occasionally cause postoperative coma as a result of hypernatraemia.[7]

The possible association between diabetes insipidus and an increased risk of hypothermia during surgery has not previously been described in the anaesthetic literature. In this case, impaired temperature regulation may have occurred secondary to hypothalamic disturbance related to the diabetes insipidus despite the absence of other clinical endocrine dysfunction.

We therefore suggest that these patients are at increased risk from hypothermia and that per- and postoperative temperature monitoring is advisable. Measures should also be taken to minimise the decrease of core temperature particularly during prolonged surgery.

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CASE REPORT

Pain after spinal intrathecal clonidine

An adverse interaction with tricyclic antidepressants?

P. A. J. HARDY AND J. C. D. WELLS

Summary

A case is reported in which spinal intrathecal administration of clonidine produced pain. The interaction between clonidine and tricyclic antidepressants is discussed, and is suggested as the basis for this observation.

Key words

Anaesthetic techniques, regional; spinal.
Pain; pathological.
Pharmacology; clonidine.

Two major descending tract systems, noradrenergic and serotoninergic, are implicated in the control of nociceptive input in the spinal cord.[1] The alpha-2 adrenergic agonist clonidine has been shown to produce analgesia in animals[2] and after both intravenous[3] and extradural[4] administration in man. We report a case in which pain was precipitated by spinal intrathecal administration of clonidine to a patient concurrently taking tricyclic antidepressants.

Case history

A 65-year-old man presented with burning perineal pain of undetermined origin which had started 6 months after curative abdominoperineal excision for carcinoma. The pain was aggravated by standing and walking but relieved by lying down. Slow release oral morphine administration had had limited effect so treatment in clinic was started with a combination of amitriptyline 75 mg at night and sodium valproate 500 mg 3 times a day. This resulted in slight improvement and he was therefore admitted for further assessment.

Bilateral lumbar sympathetic blocks were of no benefit. A differential spinal block using incremental injections of lignocaine showed that major sensory block was required to produce analgesia. A test injection of intrathecal morphine 6 mg was performed later and produced good analgesia. A Port-a-Cath intrathecal drug delivery system was implanted in view of this response and regular twice daily boluses of diamorphine 5 mg maintained good analgesia.

The patient started to complain of hallucinations and sedation after 2 weeks of good analgesia, despite a reduction in the dose of diamorphine to 1.25 mg twice a day. He was readmitted to assess alternative analgesia. Intrathecal clonidine has been used successfully in patients with opioid tolerance[5] and a test injection of 75 μg was therefore administered; the patient was not in pain at the time of injection. He was reassessed later when he was found to be in severe pain which had started within 5 minutes of the injection. The pain was similar to his earlier discomfort but this time did not respond to his lying down. However, it resolved completely 30 minutes after 5 mg intrathecal diamorphine.

Discussion

Clonidine is an alpha-2 adrenergic partial agonist which has been used both alone[4] and in combination with opioids in the treatment of acute and chronic pain, and in opioid substitution when tolerance or tachyphylaxis intervene.[5] Toxicity studies of spinal clonidine have shown it to be free from histopathological[6] and cord blood flow[7] effects. The noradrenergic pathways subserving nociception demonstrate mixed effects. Alpha-adrenoceptor blockers administered spinally antagonise morphine analgesia[8] but when administered supraspinally are analgesic.[9]

Clonidine and tricyclic antidepressants are known to interact adversely both in relation to arterial blood pressure control and in the treatment of depression.[10] The patient took regular medication which included a tricyclic antidepressant. The pharmacological profile of these drugs is a mixed aminergic re-uptake blockade, and receptor blockade with predominant activity on noradrenaline, serotonin and dopamine transmission; they also effect muscarinic cholinergic antagonism and histamine receptor activity.[10] An alteration in receptor function occurs with chronic

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administration; this increases the responsiveness of the alpha-1-adrenergic receptors[11] and desensitises the presynaptic alpha-2-adrenoceptors.[12] There is also a decrease in the number of 5HT receptors[13] and an increase in sensitivity to exogenous 5HT.[14]

Recent evidence has shown that some activity may occur on cholinergic transmission, in addition to the recognised effects of clonidine on adrenergic transmission.[15] The interactions here may be as a result of the effects of the presynaptic alpha-2-adrenoceptors on the cholinergic fibres' decreased transmitter release. Clonidine also inhibits acetylcholinesterase.

There are therefore two mechanisms which may have precipitated pain in the present case. In the first the clonidine–cholinergic interaction may be responsible. Atropine has been used to attenuate the analgesia produced by clonidine (T. Gordh, personal communication) and the muscarinic blockade of amitriptyline may therefore have attenuated the analgesia so produced. In the second the interaction may have been through the adrenergic system. The tricyclic augmentation of serotoninergic transmission at spinal level may have unmasked an effect of clonidine at central receptors to enhance nociception. A further adrenergic basis, noradrenaline re-uptake block at spinal levels, could also result in an increase in receptor-available amine. Clonidine would act as an antagonist in this microenvironment and thus enhance nociceptive input. The speed of the pain's onset in this case suggests this last explanation, although the analgesia restored by opioid would support a cholinergic basis.

In conclusion, in patients who receive tricyclic antidepressants the administration of clonidine may precipitate pain.

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Anaesthesia, 1988, Volume 43, pages 1028–1030

CASE REPORT

An unexpected functional cause of upper airway obstruction

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Summary

A case of acute respiratory obstruction in the immediate postoperative period is described in a young woman who emerged from general anaesthesia after a Caesarean section for fetal distress. She had a pregnancy complicated by disabling polyhydramnios and anxiously anticipated the birth of a child with a diaphragmatic hernia, diagnosed antenatally. The cause of the airway obstruction was functional in nature as confirmed by flexible fibreoptic laryngoscopy. The diagnosis, paradoxical vocal cord motion, has to be considered as an infrequent cause of postoperative airway obstruction; its recognition and treatment are discussed. The patient did not have a history which might have indicated its possible occurrence. It is suggested that paradoxical vocal cord movement in a more mild form may be overlooked as cause for postoperative stridor and airway obstruction.

Key words

Complications; respiratory obstruction.

Acute upper airway obstruction is a serious medical condition which requires prompt diagnosis and treatment. There is usually an organic cause for the obstruction, but an increasing number of reports have documented cases without a definite organic aetiology.[1–8] Paradoxical vocal cord motion, an abnormal motion of the vocal cords characterised by their adduction during inspiration and abduction with exhalation, has been found in several of these patients.[2,5,6] The only reported case in the anaesthetic literature concerned a patient with a longstanding history of respiratory symptomatology and previously documented episodes of paradoxical vocal cord movement who had persistent postoperative stridor which required acute intervention and prolonged intensive care.[8] We now present a case of acute respiratory obstruction due to the condition after tracheal anaesthesia in a previously healthy patient without a history of any respiratory illnesses.

Case history

A 26-year-old white female was transferred to the University Women's Hospital during her 35th week of pregnancy with the diagnosis of incapacitating polyhydramnios. Her medical history was significant for one normal vaginal delivery and a dilatation and curettage performed under general anaesthesia. Both procedures were achieved without complications. She did not have a history of asthma, upper or lower respiratory tract infections or allergies. Except for pregnancy and polyhydramnios, her physical examination was unremarkable, in particular with respect to her head and neck, upper airway and pulmonary status. She was normotensive without oedema or other signs or symptoms of pre-eclampsia. Her prepregnant weight was 68 kg while her weight at admission was 85 kg, at a height of 1.60 m.

An abdominal ultrasound confirmed the polyhydramnios, and in addition, revealed the presence of a left diaphragmatic hernia in an approximately 36-week-old fetus. An amniocentesis demonstrated an immature lecithin/sphingomyelin (L/S) ratio. She was kept in hospital and the delivery was delayed until extracorporeal membrane oxygenator support was available and the fetal lungs had matured. A mature L/S ratio was present one week later and an amniotic catheter was sited. Amniotic fluid was drained slowly over a period of 8 hours. The next day the patient had a spontaneous rupture of membranes and labour started. Internal uterine and fetal heart rate monitors were placed. The labour became irregular and dysfunctional at which time an intravenous infusion of oxytocin was started. Shortly after, late decelerations were noted on the fetal heart rate tracing. The oxytocin was discontinued and the patient was put in the left lateral decubitus position. Oxygen was given by nasal cannula. A fetal scalp pH was 7.32. The patient was managed expectantly for the next 15

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minutes and the decelerations diminished. A repeat fetal scalp pH was 7.28; fetal distress was diagnosed and an urgent Caesarean section was undertaken.

The anxious patient was given sodium citrate 30 ml by mouth and 100% oxygen by mask. General anaesthesia was induced in a 'rapid sequence' fashion with thiamylal 300 mg and suxamethonium 100 mg intravenously while cricoid pressure was maintained. The trachea was easily intubated with a 7.0 mm internal diameter, cuffed tracheal tube and anaesthesia was maintained with 50% nitrous oxide in oxygen and 0.5% halothane. The baby was delivered 5 minutes after induction; he appeared cyanotic, hypotonic, was not irritable and did not cry, but improved promptly after resuscitative measures. His Apgar scores were two and seven at 1 and 5 minutes respectively; the umbilical cord's venous blood pH was 7.33. The mother was given morphine 10 mg intravenously, and vecuronium 4 mg. The surgery proceeded uneventfully and finished 25 minutes later. General anaesthesia was discontinued and the muscle relaxant reversed with neostigmine 2.5 mg and atropine 1.2 mg.

Her trachea was extubated when she was fully awake and her muscular strength had returned as determined by the presence of an adequate tidal volume, extremity movement, and head lift. She was transferred to a stretcher while breathing well. Upon turning her to the lateral decubitus position she developed stridor followed shortly by the cessation of ventilation and signs of upper airway obstruction. The awake patient appeared in obvious distress and grasped her throat with her hands. Neck extension, jaw lifting, the insertion of a nasopharyngeal airway, and attempted positive pressure ventilation applied by way of a mask failed to relieve the obstruction and establish ventilation; her lips and nail beds became cyanotic. Laryngospasm was suspected and she was given thiamylal 300 mg and suxamethonium 100 mg, after which ventilation by mask was easy, while cricoid pressure was applied; her trachea was again intubated without difficulty with a 7.0-mm cuffed tracheal tube. No anatomical abnormalities, foreign bodies, or oedema were noted during direct laryngoscopy. Ventilation was unimpeded with bilaterally clear breath sounds; her oxygen saturation, measured by a pulse oxymeter, was 99%. She received 50% nitrous oxide in oxygen to keep her sedated until a transcutaneous nerve stimulator demonstrated the spontaneous, complete return of the train-of-four and a sustained tetanus at 100 Hz.

The nitrous oxide was discontinued, and when she was awake and responding to commands with adequate muscle strength as determined by hand grip and neck lift, she was again extubated. She developed stridor immediately, which persisted despite manoeuvres including neck extension, jaw lift and positive airway pressure by mask. The patient sat up and improved only slightly. She alternated between severe stridor and mild to moderate dyspnoea over the next 15 minutes. Her oxygen saturation remained at 98–99% on room air, however; she was able to speak intermittently in a weak hoarse voice, and affirmed to difficulty with breathing and to a 'foreign body' feeling in her throat. She was unable to cough. Lignocaine 100 mg and hydrocortisone 100 mg were given intravenously without any apparent effect. The otolaryngologists were consulted urgently and fibreoptic nasopharyngeal laryngoscopy was performed. This revealed paradoxical movement of her vocal cords with intermittent episodes of normal function. No foreign body, oedema, bleeding or other evidence of trauma was present. No attempt was made to pass the fibrescope beyond her vocal cords to avoid further compromise of her airway. The patient's varying degree of respiratory difficulty, especially upon assuming the recumbent position, the inability to rule out subglottic abnormality, and her own request led to her re-intubation and sedation overnight. Ventilation was unassisted throughout the night. A chest X ray demonstrated the tracheal tube to be in a satisfactory position; no pulmonary abnormalities were noted.

A direct laryngoscopy and a bronchoscopy were performed under general anaesthesia the next day. No anatomical abnormalities, evidence of trauma, oedema, or infections were found. The patient breathed well after extubation while sedated; however, once she was fully awake in the recovery room, she developed a mild stridor, which disappeared after the patient was given reassurance. An interview with her husband revealed that the patient had been very tense and anxious in the weeks preceding her operation because of difficulties experienced during pregnancy. There was no history of psychiatric problems or of previous episodes that would suggest a conversion disorder. The patient returned to the obstetric service and was discharged in good condition 4 days later.

Discussion

Upper airway obstruction from paradoxical vocal cord movement may resemble airway obstruction from other causes; it must be differentiated from laryngospasm, foreign body aspiration, vocal cord paralysis, allergic reactions, trauma, infection, oedema, and tumours. Patients with the condition have been treated for uncontrollable asthma, anaphylaxis, laryngospasm, and vocal cord paralysis. Thus it is not surprising that several of the patients with this functional disorder have received aggressive therapy which included high dose steroids, tracheal intubation, and tracheostomy.[4,5,7,8] The diagnosis is made by evaluation of vocal cord motion during an attack. Appropriate therapeutic manoeuvres may be applied before having to resort to drastic treatment once the correct diagnosis has been reached. Most of the cases of paradoxical vocal cord movement, confirmed by laryngoscopy, have responded to verbal support, placebo treatment, phonation therapy, or psychological support.[5] Focused professional attention on the seriousness of the respiratory symptomatology of paradoxical vocal cord movement may magnify the symptoms as it reinforces the conversion reaction.

There appear to be several elements common to patients with this diagnosis. The majority have been women in the 18–50 age range who develop stridor or signs of upper airway obstruction, become tachypnoeic, contrary to what would be expected with an inspiratory obstruction, have a weak or absent voice, and are unable to cough.[3,5] Arterial blood gases have been largely normal during attacks.[3,7] The patients improved with the treatment described above, and psychological evaluation revealed a variety of psychiatric disorders with conversion elements. The patients are not consciously aware of the problem, and typically, cannot simulate the condition voluntarily.[5,7] The episode in some of them had been preceded by an upper respiratory tract infection or a surgical procedure with general anaesthesia. This led Kellman and Leopold to suggest that the upper respiratory tract infection or tracheal intubation may direct a patient's attention to the larynx.[5]

The case presented here has several of the common elements described previously, including age, sex, characteristics of the obstruction, laryngeal findings, and the response to verbal support. She experienced psychological stress in the immediate peripartum period, but she did not have a history of conversion reactions, psychiatric disorders, respiratory disease or paradoxical vocal cord movement, unlike a previous case described in conjunction with general anaesthesia.[8] She had been under a significant amount of stress and it is indeed possible that the presence of a tracheal tube directed her attention to the larynx when she woke up after surgery. A complete psychological evaluation was not carried out. We were concerned about the potential for aspiration so the tracheal tube was kept in place until she was fully awake. The symptoms became apparent only after extubation. Sedative therapy with benzodiazepines or narcotics might have been a therapeutic alternative at that time, but sedation has had variable success and may fail and compromise the patient in the postoperative period.[7,8] Intubation and extubation at a deep level of anaesthesia has been advised in patients who have a history of the condition.[8] However, once the patient emerges from general anaesthesia, it may again present itself. Furthermore, as exemplified in this report, extubation at a deep level of anaesthesia may not be advisable. We elected to re-intubate the patient as a temporary measure to allow for postoperative stabilisation and further evaluation.

Recently, we cared for a 31-year-old woman who presented for a diagnostic laparoscopy. She had a history of stridor which developed after a previous laparoscopy and subsided with oxygen delivery by mask, and verbal reassurance. The patient underwent an uneventful surgical procedure under general tracheal anaesthesia and was extubated at the end of the case. She developed stridor and became anxious and tachypneic upon arrival in the recovery room, but remained well oxygenated. She was able to speak in a weak voice. Paradoxical vocal cord movement was suspected, but fibreoptic laryngoscopy was not available to confirm the diagnosis. She was given verbal support with instructions to concentrate on the expiratory phase of her respiratory cycle. The stridor disappeared with these measures. It recurred 20 minutes later, and again responded to verbal support. The patient was discharged home the same day in good condition. We suspect that this case was also caused by paradoxical vocal cord movement, even though we were unable to confirm it.

In milder forms the problem may be overlooked and be more common than generally acknowledged. If this is true, anaesthetists are likely to see patients with paradoxical vocal cord movement. Thus it should be considered in the differential diagnosis of postoperative stridor and respiratory obstruction; an increased awareness of this disorder should help to treat it correctly. However, the diagnosis should only be made after other causes of airway obstruction have been ruled out and the characteristic findings identified at laryngoscopy. We suggest further that if verbal reassurance and placebo intramuscular injections fail to relieve the symptoms, the administration of antipsychotic medications (haloperidol, droperidol) may also be considered in the acute phase as a temporary measure.

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CASE REPORT

Phaeochromocytoma—a presentation mimicking malignant hyperthermia

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P. G. COLLINS

Summary

A 52-year-old apparently healthy, normotensive woman who presented for elective cholecystectomy experienced intra-operative hypertension and tachycardia, which were controlled by propranolol. Oesophageal temperature increased, there was a metabolic and respiratory acidosis with hypoxaemia, and malignant hyperthermia was diagnosed. Severe cardiogenic pulmonary oedema ensued, and was treated with intravenous glyceryl trinitrate. Ventricular fibrillation caused cardiac arrest, and this was treated successfully. Postoperatively a phaeochromocytoma was discovered, and removed at a subsequent operation. The case illustrates the similarities in presentation of malignant hyperthermia and phaeochromocytoma, and the possibility that misdiagnosis may exacerbate the crisis.

Key words

Hyperthermia; malignant.
Surgery; phaeochromocytoma.

Malignant hyperthermia and phaeochromocytoma are rare conditions which may present during anaesthesia, with serious consequences. Failure of prompt recognition and appropriate treatment may jeopardise outcome.

Case history

A 52-year-old 65 kg woman presented for elective cholecystectomy. History and examination were normal apart from menopausal symptoms, for which she was taking oestrogen replacements. There was no history of previous surgery, anaesthesia, hypertension or diabetes. Family history was negative for complications of surgery. Arterial pressure was 110/70 mmHg on the day before surgery, and three other normal readings had been recorded previously. Heart rate was 80 beats/minute. Haemoglobin, electrolytes, urinalysis and electrocardiograph (ECG) were normal. Anaesthesia comprised fentanyl 200 μg, thiopentone 250 mg, suxamethonium 100 mg, pancuronium 6 mg, nitrous oxide 66% with oxygen and enflurane. Positive pressure ventilation was adjusted to maintain an end-tidal $P\text{CO}_2$ of 4.7 kPa. ECG and cuff blood pressures were monitored.

Systolic arterial pressure increased to 190 mmHg and heart rate to 145 beats/minute when the peritoneum was opened. The skin was sweaty and the surgeon remarked that the abdomen was tight. Oesophageal temperature was 36.7°C, and this allayed fears of malignant hyperthermia. The tachycardia and hypertension were controlled by an increase in depth of anaesthesia. Hypertension and tachycardia recurred on dissection of the gall-bladder bed, and persisted throughout cholecystectomy. Palpation of the adrenal glands revealed no tumours. The possibility of phaeochromocytoma was thought unlikely, and consequently propranolol was given to a total of 2 mg to control arterial pressure and heart rate.

Paralysis was reversed with neostigmine 2.5 mg and glycopyrronium 0.5 mg. Shortly afterwards, the patient became cyanosed; the temperature had increased to 38.3°C. A provisional diagnosis of malignant hyperthermia (MH) was made and treatment with cooling, bicarbonate and dantrolene was started. Arterial blood gas analysis showed a $Pa\text{O}_2$ of 8.2 kPa ($F\text{IO}_2$ 1.0), $Pa\text{CO}_2$ 7.5 kPa, bicarbonate 17 mmol/litre and pH 7.22. Severe pulmonary oedema and peripheral vasoconstriction became evident. Ventricular tachycardia ensued and proceeded to ventricular fibrillation, which was treated successfully by DC shock. A pulmonary artery catheter was inserted; pulmonary artery pressure was 60/40 mmHg, and pulmonary capillary wedge pressure 29 mmHg. Intravenous glyceryl trinitrate was started by infusion and this improved peripheral perfusion and reduced pulmonary oedema. Cardiac output measured during the glyceryl trinitrate infusion was 2.25 litres/minute, and systemic vascular resistance 3050 dynes second/cm^5 (normal 600–1200).

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Postoperatively, the lungs were ventilated mechanically for 48 hours; the pulmonary oedema resolved within 24 hours. There was no recurrence of the hypertension after the cardiac arrest, although sinus tachycardia persisted for 24 hours. There was elevation of the serum potassium concentration to 5.6 mmol/litre, but this decreased by 24 hours to 2.8 mmol/litre. Muscle enzymes were elevated; creatine phosphokinase was eight times normal (MB fraction 2%), aldolase four times normal, and lactate dehydrogenase 3.5 times normal. Prothrombin time was prolonged to 23/15 sec.

Ischaemia in the distribution of the right radial artery developed 12 hours postoperatively; the ipsilateral brachial artery cannula (for which a cut-down and insertion under direct vision had been necessary) was removed. Exploration and arteriography showed severe vasospasm, which responded to stellate ganglion blockade. Urinary metanephrines, measured in the first 24 hours postoperatively, were greatly elevated at 9.4 mg/24 hours (normal up to 1.3 mg); plasma adrenaline was 1200 pg/ml (normal 50–100), and plasma noradrenaline was 4800 pg/ml (normal 200–400). Ultrasound scan of the kidneys and computerised tomography showed a 2.2 cm diameter phaeochromocytoma in the left adrenal gland. Alpha- and beta-blockade were instituted.

The phaeochromocytoma was resected successfully 21 days after cholecystectomy. Postoperative recovery was uneventful. The only sequela was temporary unilateral impairment of visual acuity after the phaeochromocytoma crisis, ascribed to retinal vasospasm, and this resolved completely.

Discussion

Many features of this case suggested a diagnosis of MH; an increase in temperature, tachycardia, metabolic and respiratory acidosis, ventricular irritability, hyperkalaemia, increase in muscle enzymes and a coagulopathy. The drugs used included suxamethonium and enflurane, which are known MH trigger agents. Cholecystectomy is not an operation associated particularly with MH,[1] but cholelithiasis is a common accompaniment of phaeochromocytoma.[2] The lack of rigidity as in this case should not be used as an argument against a diagnosis of MH; rigidity is absent in 25% of instances of MH.[3]

The rate of temperature increase (1°C/hour in this case) was not of the alarming degree seen classically in MH, but smaller rates of increase have been described when heat loss is increased or cardiac output is low.[3] The pyrexia and sweating in this case can be ascribed to the increased metabolic rate that results from catecholamine excess,[4] and not to humoral stimulation of sweat glands which are innervated by cholinergic fibres. Plans to refer the patient to another centre for muscle biopsy were cancelled after diagnosis of the phaeochromocytoma by elevated catecholamines and imaging of the tumour, as it was felt that all the patient's problems could be explained by a secreting phaeochromocytoma.

Hypertension and severe peripheral ischaemia are not features of MH. Moderate hypoxaemia occurs in MH,[1] but not the severe pulmonary oedema that occurred in this patient. Acute limb ischaemia has been described in phaeochromocytoma,[5] and hypertension is a hallmark of the disease. Phaeochromocytoma that presents during anaesthesia for unrelated surgery was said to carry a 50% mortality in 1951;[6] there are no more recent figures to refute this.

Two active measures in this case may have promoted the severity of the crisis. Palpation of the adrenals is known to provoke catecholamine secretion (and failed to identify the tumour in this case). Propranolol has induced pulmonary oedema in phaeochromocytoma,[7] and is contraindicated in such cases without prior adequate alpha-adrenergic blockade.[8] The nonselective beta-blocker propranolol causes an increase in systemic vascular resistance because it inhibits beta-mediated vasodilatation, and leaves alpha-mediated vasoconstriction unopposed; in addition it has a negative inotropic effect. This patient had normal cardiac contractility as measured by left ventricular stroke work index; grossly increased systemic vascular resistance was the major cause of her low cardiac output.

Misdiagnosis and inappropriate medication contributed to the severity of this crisis. Administration of the relatively harmless dantrolene cannot be blamed for any ill-effects, except expense and waste of time. Insertion of the pulmonary artery catheter led to the appropriate use of glyceryl trinitrate although the cause of the vasoconstriction was not known. Fortunately, the patient survived unharmed, and consequently this lesson in differential diagnosis was less painful for those involved.

Lack of prior hypertension and glycosuria do not exclude a diagnosis of phaeochromocytoma, and in the event of inability to differentiate MH from phaeochromocytoma, supportive treatment common to both is possible (cooling, bicarbonate, dantrolene and vasodilatation). Beta-blockade and adrenal palpation are contraindicated.

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Anaesthesia, 1988, Volume 43, pages 1033–1034

CASE REPORT

Haemoglobin H disease and cardiac surgery

S. J. ROWBOTTOM AND D. A. SUDHAMAN

Summary

The management of two patients with haemoglobin H disease, who underwent open-heart surgery, is described and the problems that relate to anaesthesia in the presence of this condition are discussed.

Key words

Anaesthesia; cardiac.
Co-existing disease; thalassaemia, haemoglobin H disease.

Haemoglobin H (HbH) disease is a haemolytic alpha thalassaemia in which haemolysis may be provoked by infection or a number of oxidant drugs which include sodium nitroprusside.[1,2] Additionally, precipitation of the HbH molecule can occur at cold temperatures.[2]

Haemolysis is a recognised sequela of cardiopulmonary bypass (CPB) and commonly results from mechanical trauma, contact with artificial surfaces and an increase in red cell membrane fragility.[3] The deleterious effects of CPB on red cells may be exacerbated in patients with haematological disorders.[4] We present two patients with HbH disease who underwent open-heart surgery and discuss the possible anaesthetic complications.

Case histories

Case 1

A 52-year-old Chinese woman with chronic rheumatic heart disease and haemoglobin H disease was scheduled for mitral valve replacement. Physical examination showed her to be anaemic and slightly jaundiced with mild hepatosplenomegaly. She was in controlled congestive heart failure with atrial fibrillation and the murmurs of mixed mitral valve disease. A chest X ray and ECG supported these findings. Cardiac catheterisation and echocardiography confirmed the presence of mixed mitral valve disease with predominant mitral regurgitation and mild pulmonary hypertension.

Routine blood and urine tests showed a mild chronic haemolytic anaemia (Table 1). Anisocytosis, poikilocytosis and polychromasia were seen on a blood film and haemoglobin H was present on a brilliant cresyl blue smear. Plasma haemoglobin was measured at 40 mg/100 ml (normal range is 0.5–2.5 mg/100 ml).[5] Serum urea and electrolytes, liver function tests and clotting studies were normal. Daily medications were digoxin 0.125 mg and frusemide 40 mg orally.

Table 1. Blood and urine tests.

	Case 1	Case 2
Haemoglobin	9 g/litre	10 g/litre
Packed cell volume (PCV)	0.27	0.36
Mean corpuscular volume (MCV)	65 flitre	72 flitre
Mean corpuscular haemoglobin (MCH)	22 pg	20 pg
Mean corpuscular haemoglobin concentration (MCHC)	23 g/dlitre	29 g/dlitre
Reticulocytes	4.1%	5.4%
Plasma bilirubin	48 μmol/litre	33 μmol/litre
Urobilinogen	present	present
Haemosiderinuria	present	present

Anaesthesia was induced with diazepam and maintained by pancuronium, morphine and isoflurane in 50% oxygen/nitrous-oxide after premedication with diazepam given orally and morphine sulphate given intramuscularly. The mitral valve was replaced with a Carpentier-Edwards bioprosthesis. The procedure was performed using a Bentley 10 oxygenator, hypothermia to a rectal temperature of 28°C, haemodilution to a packed cell volume (PCV) of 0.25 with a pump flow rate of 2.4 litres/minute/sq m. Ice cooled crystalloid cardioplegic solution that contained 20 ml St. Thomas's solution per litre was used to arrest the circulation. The pump circuit was primed with 800 ml of

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whole blood and 700 ml of Ringer-lactate solution. The plasma haemoglobin levels of the pump prime at the beginning and end of bypass were 20 mg/100 ml and 80 mg/100 ml, respectively. Mild haemoglobinuria developed towards the end of the procedure. The duration of bypass was 59 minutes.

The haemoglobinuria resolved rapidly after operation with no evidence of exaggerated intravascular haemolysis as monitored by haemoglobin, bilirubin levels and a blood film. Blood tests a month later still showed a hypochromic microcytic anaemia with mild haemolysis.

Case 2

A 35-year-old Chinese male had chronic rheumatic heart disease and HbH disease and had previously undergone a cholecystectomy for pigment gallstones and a splenectomy to control haemolysis.

He was anaemic and slightly jaundiced on examination. The heart was enlarged, in sinus rhythm, and murmurs of mitral stenosis and aortic incompetence were present. Cardiomegaly was present on a chest X ray and the ECG showed P mitrale only. Cardiac catheterisation and echocardiographic studies revealed severe mitral stenosis, pulmonary hypertension (60/35 mmHg) and mild aortic regurgitation. Blood and urine tests (Table 1) showed a mild haemolytic anaemia. A band of HbH was present on electrophoresis. Plasma haemoglobin was measured at 30 mg/100 ml. A blood film was reported to show hypochromic, microcytic red cells with polychromasia, anisocytosis and target cells.

Premedication using oral lorazepam and intramuscular morphine sulphate, was followed by anaesthesia induced with midazolam and fentanyl, and maintained by pancuronium and isoflurane in 50% oxygen, nitrous oxide. Sodium nitroprusside was used to control hypertension before bypass; a total of 2 mg was given. An open mitral valvotomy was performed using the same bypass technique as in Case 1. The prime consisted of one litre fresh blood and one litre Ringer-lactate solution. The plasma haemoglobin levels of the prime at the beginning and end of bypass were 16 mg/100 ml and 24 mg/100 ml. The duration of bypass was one hour. The postoperative course was uneventful.

Discussion

Haemoglobin H disease is an alpha thalassaemia; an inheritable disorder of haemoglobin chain synthesis in which there is a reduction of alpha globin chains. The disorder mainly affects Orientals and is primarily a haemolytic state with some impairment of erythropoiesis. Red cells contain a variable proportion of HbH and normal haemoglobin (HbA). Haemolysis results from an abnormality of red cell membrane permeability caused by the presence of intracellular inclusions (Heinz bodies). The reduction in globin chain synthesis leads to a hypochromic, microcytic anaemia. Anisocytosis, target cells, and inclusions are seen on a blood film with a mild reticulocytosis.[2]

The molecular differences between HbH and normal adult haemoglobin (HbA) have some practical implications. Haemoglobin H has an affinity for oxygen 10 times that of normal haemoglobin; its oxygen dissociation curve is shifted to the left of normal, and is shaped like a rectangular hyperbola. Consequently HbH contributes little to oxygen transport. Oxidant drugs and infections can precipitate haemolysis and worsen oxygen delivery.[2] Oxidant drugs related to anaesthetic practice include: prilocaine, sodium nitroprusside, sulphonamides, penicillin, chloramphenicol, vitamin K and aspirin.[5] The use of a small amount of sodium nitroprusside in Case 2 was not seen to initiate haemolysis but this would have been masked by the use of cardiopulmonary bypass shortly afterwards. Additionally, the HbH molecule is thermolabile and precipitates if left at 4°C. Theoretically the use of cold cardioplegic solutions could cause intracoronary precipitation, inadequate distribution of cardioplegic solution, and result in myocardial ischaemia or infarction. There was, however, no ECG or cardiac enzyme evidence of this postoperatively in either patient. Presumably the bypass time of one hour in both cases was insufficient for precipitation to occur.

The heart may be affected by an acquired haemachromatosis, secondary to chronic haemolysis or repeated blood transfusions. Cardiac failure, arrhythmias and disturbance of conduction develop. Pericarditis with pericardial effusions are found in 50% of patients.[6,7] Bone marrow hyperplasia secondary to chronic haemolysis can result in thalassaemic facies[2]—a prominent maxilla and sunken nose—which has led to difficulties in visualising the glottis.[8] This was not a problem here.

Average plasma haemoglobin levels of 40–50 mg/100 ml were measured after 2 hours of bypass surgery in patients undergoing coronary artery bypass grafting.[9] The plasma haemoglobin level of patient 1 after approximately one hour of bypass was greater than this, although the initial value was 40 mg/100 ml. Whether this represents a minor exacerbation of the haemolytic trait is conjectural since the haemoglobinuria resolved rapidly and there was no evidence of a sustained increase in haemolysis.

In conclusion, patients with HbH disease can undergo a standard cardiopulmonary bypass technique and sodium nitroprusside may be used in small amounts.

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APPARATUS

Evaluation of a multigas anaesthetic monitor: the Datex Capnomac

H. McPEAK, E. PALAYIWA, R. MADGWICK AND M. K. SYKES

Summary

A laboratory investigation was carried out to evaluate the performance of the Datex Capnomac multigas anaesthetic agent analyser, with particular emphasis on accuracy, response and delay times, zero and gain stability and interference from water vapour. The analysis of anaesthetic vapours was less accurate than the analysis of CO_2, O_2 and N_2O, but acceptable for clinical use. The response to square wave changes in gas composition was accurate at frequencies up to 60 per minute for CO_2 and 30 per minute for O_2, but with N_2O and the anaesthetic vapours there was a decrease in accuracy at frequencies above 20 breaths/minute. The instrument appeared to be unaffected by water vapour.

Key words

Equipment; analysis.

The Datex Capnomac is a microprocessor-controlled multigas anaesthetic monitor designed for use in the operating theatre. It is claimed that the response time of the analyser is fast enough to permit breath-by-breath analysis of oxygen, carbon dioxide and nitrous oxide, as well as the anaesthetic vapours halothane, enflurane and isoflurane. This report describes a laboratory evaluation of the performance of this device.

Description of the instrument

The Capnomac is mains powered. The dimensions are 340/330/165 mm, and the weight is 11 kg. Power requirements are 100/115/220/240 volts, 50/60 Hz. The Capnomac has digital displays for,

End-tidal CO_2 as a percentage or partial pressure in mmHg.
Mean end-tidal CO_2 over the last 15 minutes as a percentage or partial pressure in mmHg.
Inspiratory O_2 percentage.
Inspiratory (or expiratory) N_2O percentage.
Respiratory rate.
Breath by breath inspiratory/expiratory O_2 difference.
Inspired and expired anaesthetic concentration.
On the left hand side of the instrument a LED-bar graph displays the variation in CO_2 concentration on a breath-by-breath basis and below this there is a panel for the display of alarm messages (Fig. 1).

There are a number of controls operated by touch switches on the right-hand side of the panel. The display key serves three functions. First, it turns the displays for mean end-tidal CO_2, inspired or end-tidal N_2O, respiratory rate and inspired-expired O_2 % on or off. Second, when used in conjunction with the CO_2 key, the digital end-tidal CO_2 display can be set to read either percentage or mmHg CO_2. Third, when used in conjunction with the N_2O key, the inspired N_2O can be changed to end-tidal N_2O and *vice versa*. These choices are indicated by the addition of FI or Et to the display. There are adjustable high/low alarm levels for end-tidal CO_2, inspired O_2, inspired N_2O and anaesthetic agent, and a message field for 'apnoea', 'alarms off' and 'occlusion' indicators.

The volume of the watertrap is 9.0 ml. External connexions at the rear of the instrument provide a parallel trend output for a printer, an RS 232C data output and an analog output for O_2, CO_2 and N_2O or anaesthetic vapour. A modification is available which enables all four variables to be recorded simultaneously.

Principles of measurement

CO_2, N_2O and anaesthetic vapours

The measurements are based on the absorption of infrared radiation. All gases with two or more different atoms in the molecule absorb infrared radiation to a varying extent, the absorption pattern being specific for each gas.

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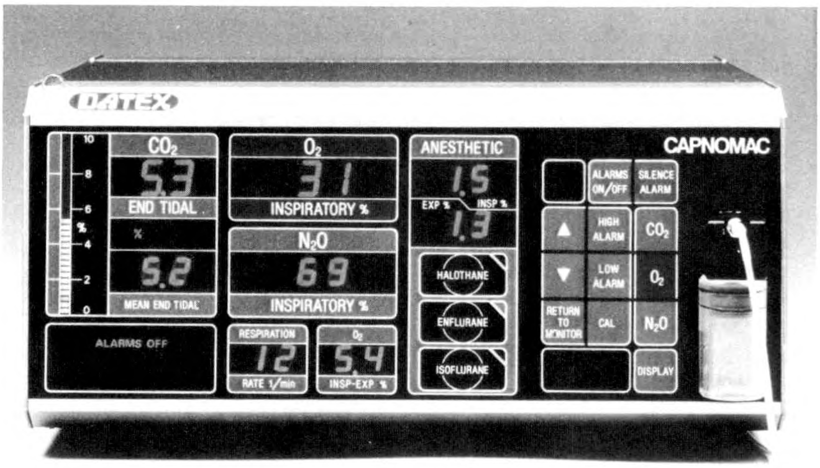

Fig. 1. The Datex Capnomac, front panel.

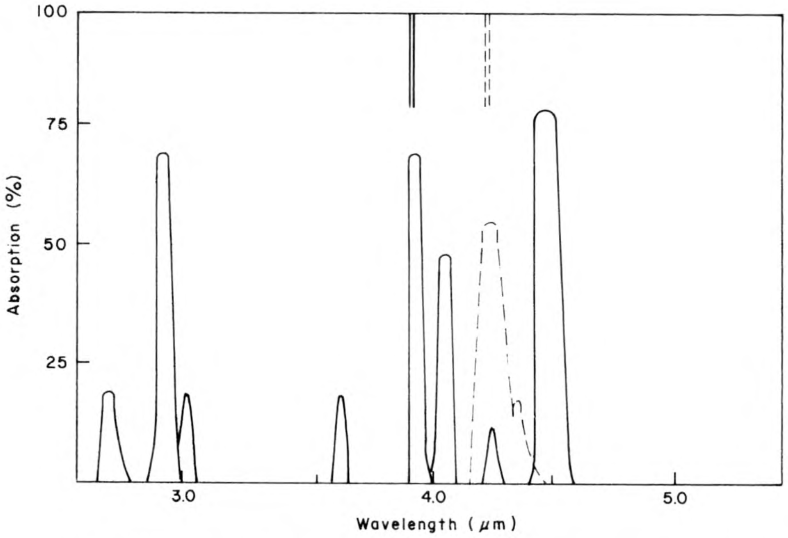

Fig. 2. Absorption spectra for N_2O and CO_2. Filter transmittance, (——) N_2O; (- - -) CO_2.

Absorption by any gas is proportional to the number of molecules of the gas in the light path, and if the pressure in the sample cell is constant the degree of absorption will be proportional to the concentration of the gas or vapour. The absorption pattern of each gas or vapour is specific, but there is often an overlap between absorption spectra and this may make it difficult to analyse for one gas in the presence of others. A further difficulty is that the presence of one gas may alter the absorption spectrum of another by collision broadening.[1,2] Specificity can be achieved by carefully restricting measurements of absorption to a single narrow waveband, or pattern of wavebands, at which the other gases do not absorb. The absorption spectra for N_2O and CO_2 are shown in Figure 2. Those for halothane, enflurane and isoflurane are shown in Figure 3. In this instrument N_2O is measured at 3.9 μm, CO_2 at 4.3 μm (where there is also slight absorption by N_2O) and the anaesthetic vapours are all measured at 3.3 μm.

Oxygen

The O_2 analyser is based on the paramagnetic response of oxygen molecules, which are attracted into the centre of a magnetic field (Fig. 4). The sample gas and the reference gas (room air) are conducted through separate tubes into a gap in a strong electromagnetic field that is rapidly switched on and off. The forces acting on the oxygen molecules in the magnetic field create an alternating pressure difference between the two tubes, which is measured with a differential pressure transducer, the output signal being amplified to produce a DC-voltage directly proportional to the oxygen partial pressure difference between the analysis and reference tubes.

The system

Special tubing is used throughout the measuring and sampling system in order to minimise absorption of anaesthetic vapours. A pump draws the gas sample at a flow rate of 200 ml/minute through the measuring chambers for CO_2/N_2O, anaesthetic vapours and O_2 in sequence. The two chambers for measurement of CO_2/N_2O and the anaesthetic vapours contain an infrared source, a channel containing the gas to be analysed and a reference channel containing air. The reference channel for the CO_2/N_2O chamber is sealed and that for the vapours and O_2 is open

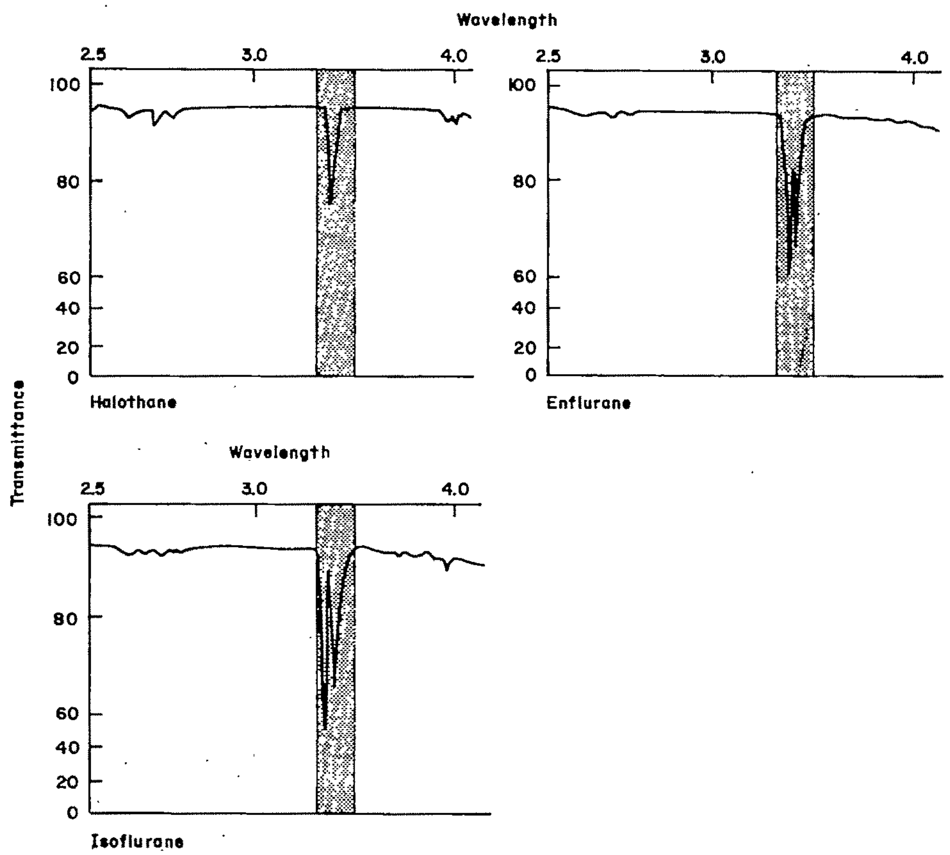

Fig. 3. Absorption spectra for the three anaesthetic vapours. ▨, measuring band.

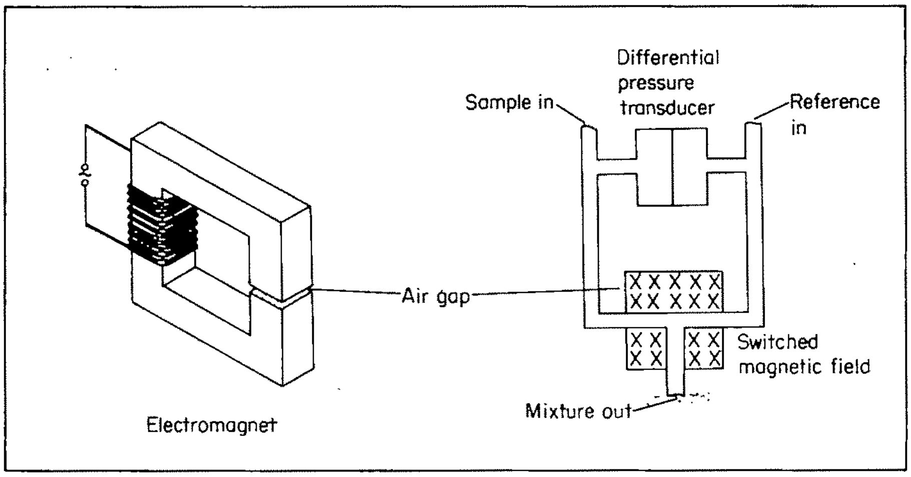

Fig. 4. The O_2 measurement principle.

to atmosphere. Infrared radiation emerging from these channels passes through a rotating disc shutter, which incorporates the narrow waveband filters. The radiation passing through the filters is then focused by a concave mirror onto a solid state detector, which measures the intensity of radiation emerging from each channel.

The pump expels the sample through the rear of the instrument and an attachment is available which permits the sample to be returned to the breathing system.

Calibration

After the instrument has been turned on and warmed up for 5 minutes, the 'cal' key is pressed for 5 seconds. The instrument samples air and automatically establishes the minimum point for each gas: CO_2–0.0%; O_2–21.0% and N_2O–0.0%. The calibration of the instrument is then adjusted by sampling known concentrations of: CO_2 (> 3%); O_2 (> 5.0%); N_2O (> 30%) and enflurane (> 2%). A Datex 'Quick Cal' Capnomac calibration canister can be used for this purpose. This contains known concentrations of the first three gases and $Freon_2$, the latter having infrared absorption peaks within the same wave band as the anaesthetic vapours (measuring band 3.3 μm–3.5 μm).

When the message 'IN' appears on the 'MEAN $ETCO_2$'

Table 1. Calibration standards used to test Datex Capnomac.

0–10% CO_2 in air, O_2 or 30% O_2/70% N_2O	Wösthoff pump, cylinders of O_2, CO_2, N_2, N_2O, CO_2
0–100% O_2 in N_2	
0–100%O_2 in N_2O	

Volatile agents by Riken refractometer: refractive powers at 760 mmHg and 22°C: halothane 1456; enflurane 1425; isoflurane 1420; N_2O 472; O_2 252.

display, the instrument is ready to receive the calibration gas. The sample tube is then inserted into the calibration gas until an audible bleep is heard and a flashing 'C' appears on the display of the gas to be calibrated, which is selected by pressing the appropriate key. The Capnomac analyses the calibration gas concentrations, enters the values into the memory and shows a value on the digital display. If this is incorrect the value on the display is adjusted to match the known concentration of the calibration gas, by pressing the 'UP or 'DOWN' arrow keys as appropriate.

This procedure is repeated for all the gases to be calibrated. After the calibration procedure 'RETURN TO MONITOR' is pressed. This returns the monitor to the measuring mode, the sensitivities are stored in the memory and the instrument is ready for use. It has been suggested that recalibration of the instrument should be performed weekly.

Laboratory evaluation

The evaluation was carried out on an instrument loaned by the suppliers. The analyser was calibrated with the 'QUICK CAL' canister at regular intervals whilst accuracy, gain stability and response times of the instrument were assessed. The effect of added water vapour was also measured.

Accuracy

The methods used to provide calibration standards are summarised in Table 1. A Wösthoff pump was used to supply known concentrations of CO_2 in the 0–10% range using air, O_2 and 30% O_2/70% N_2O as background gases. The pump was also used to provide mixtures of 0–100% O_2 in N_2 and 0 to 100% N_2O in O_2. Various concentrations of anaesthetic vapour in O_2 were generated by passing the carrier gas through Abingdon PPV vaporizers and the vapour concentrations were measured with a mass spectrometer. This was an eight-channel quadrupole instrument (Centronic MGA 200), with a standard capillary. Four channels were used for simultaneous measurement of nitrogen, oxygen and nitrous oxide on mass numbers 28, 32 and 30 and for the three vapours, halothane, enflurane and isoflurane on mass numbers 117, 51 and 51 respectively. A subtraction box similar to that described by Davis and Spence[3] was used to correct for the interference of nitrous oxide with the nitrogen and oxygen signal. The nitrogen and oxygen signals of the mass spectrometer were calibrated using room air and 100% N_2O was used to calibrate the N_2O channel. The subtraction box was set up using 100% N_2O. The calibrated channels were then switched into ASC (automatic sensitivity control) mode, which corrects for any drift in gain of the instrument and adjusts each channel output proportionally to ensure that the total is 100%.

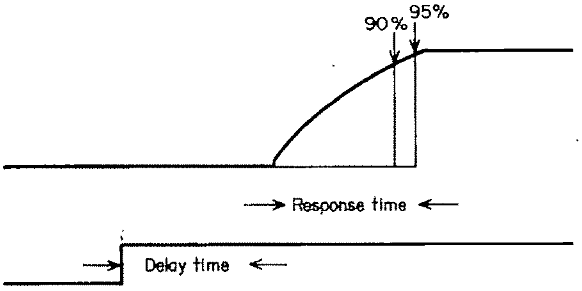

Fig. 5. Delay and response times, measured by creating a square wave change in gas concentration.

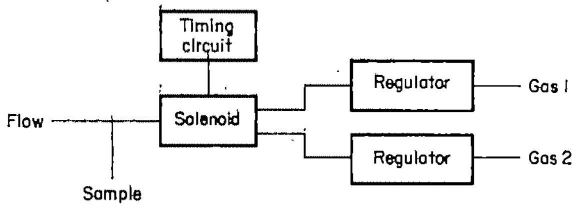

Fig. 6. Diagram of solenoid valve system used to create a square wave change in gas or vapour concentration.

To calibrate the vapour channel, oxygen was passed through a vaporizer to give a concentration of 2.8% for halothane, 1.7% for enflurane and 2.1% for isoflurane. This was analysed using a Riken optical refractometer. If x is the vapour concentration, the gain of the mass spectrometer was set to read $100x/(100 - x)$ out of ASC. When switched into ASC the reading became x%v/v. The calibration was checked with the refractometer at different vapour concentrations, to ensure that the response of the mass spectrometer was linear to within 0.1% v/v.

The refractometer used was calibrated by the manufacturer to read %v/v of halothane in O_2. The calibration factor for any agent in O_2 is proportional to the difference between the refractive power of the agent and that of oxygen.[4] The calibration factors for the other agents were therefore calculated using the refractive power values shown in Table 1.

Zero and gain stability

The long term gain stability was assessed by checking the zero and calibrating the Capnomac with the 'QUICK CAL' canister, and repeating the zero and calibration checks after a period of 18 hours during which the instrument was sampling room air.

Response and delay times

The sample delay time (time from the change in gas concentration at the tip of the sample tube to a change in concentration recorded by the analyser) and the 90 and 95% response times (Fig. 5) were measured by creating a square wave change in gas concentration using the device shown in Figure 6. The high and low concentration gas mixtures were fed into the two input ports of a three-way solenoid valve, the input pressures being adjusted to approximately 34 kPa by two regulators. The solenoid valve

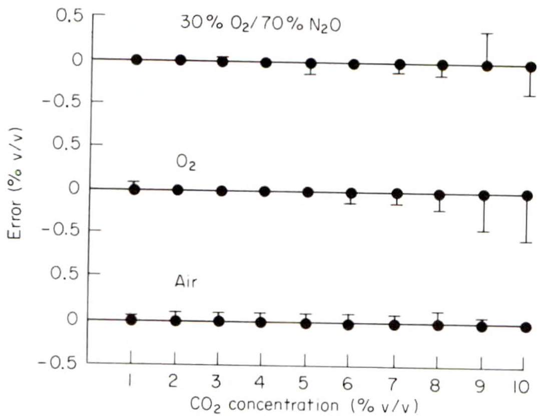

Fig. 7. Measured errors shown by horizontal bars observed during measurements on known concentrations of CO_2 in air, O_2 and 30% O_2/70% N_2O produced by a Wösthoff pump. Calibration of the Capnomac was performed with the 'QUICK CAL' cannister.

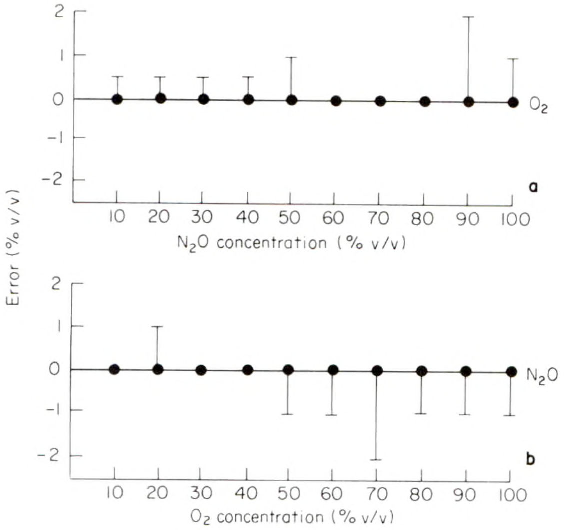

Fig. 8(a). Accuracy of measurement of N_2O concentrations in O_2. **(b).** Accuracy of measurement of O_2 concentrations in N_2O. The errors are shown by horizontal bars.

was connected to a timing circuit which produced pulses of gas of equal duration at frequencies between 5 to 60 cycles per minute. The gas issuing from the solenoid valve entered a short length of pvc-tube (ID 4 mm, length 5 cm) into which the tip of the sampling catheter was inserted. In order to ensure that the flow of the high and low concentration gases were similar the flow in the tube issuing from the solenoid valve was measured using a Fleisch pneumotachograph (size 00). Any inequalities in flow were eliminated by adjustment of the pressure regulators supplying the input gases. Measurements were made with the following pairs of gases: 100% O_2 and 95% O_2/5% CO_2;0% halothane and 3% halothane in O_2. Data on the N_2O delay and response were obtained, but no data could be obtained on the effect of breathing frequency because a fault developed in the N_2O recorder output.

Interference by water vapour

The effect of water vapour on the measured concentrations of CO_2, O_2 and N_2O was determined by bubbling the gas mixture (derived from the Wösthoff pump) through an Adams tonometer[5] filled with water at 37°C. Measurements of the relative humidity of the gas mixture issuing from the tonometer taken with a Vaisala HMI31 humidity measuring instrument showed that the relative humidity exceeded 98% at 37°C. Enflurane vapour mixtures were saturated with water vapour with a spiral coil humidifier from a Radiometer blood-gas apparatus,[6] which had a lower resistance to flow than the Adams tonometer. This device also produced almost full saturation at 37°C.

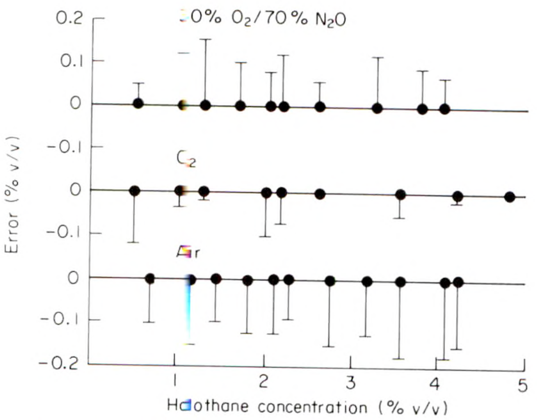

Fig. 9. Accuracy of measurements of halothane concentration in air, O_2 and 30% O_2/70% N_2O. The errors are shown by horizontal bars.

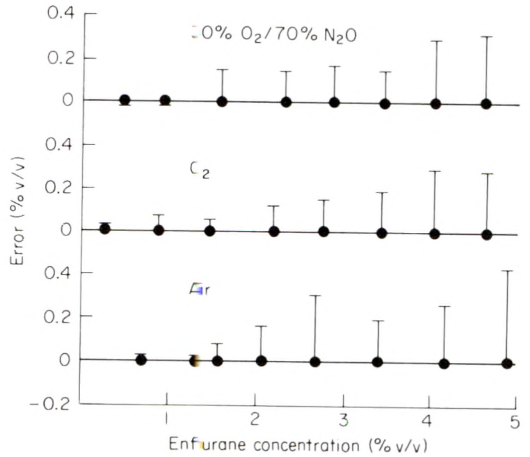

Fig. 10. Accuracy of measurement of enflurane concentration in air, O_2 and 30% O_2/70% N_2O. The errors are shown by horizontal bars.

Results

Accuracy

A comparison of the Capnomac readings against known concentrations of 0–10% CO_2 in air, O_2 and 30% O_2/70% N_2O is shown in Figure 7. The readings for CO_2 in air were accurate throughout the range, but there were errors with the other two carrier gas mixtures above 6% CO_2. Similar results were obtained whether the instrument was calibrated with the 'QUICK CAL' mixture or with 6% CO_2 in air.

The analysis of N_2O in O_2 was accurate to within 2% v/v N_2O from 0–100% N_2O, whether the analyser was calibrated with the 'QUICK CAL' canister or with 100% N_2O (Fig. 8a). The readings for O_2 concentration from 0–100% v/v displayed a similar accuracy (Fig. 8b). The error

Table 2. Response and delay times.

Gas/vapour	Response times (msec)		Delay times (msec)
	10–90%	0–95%	
Carbon dioxide	210	290	310
Oxygen	290	450	1590
Nitrous oxide	370	610	730
Halothane	730	1110	580

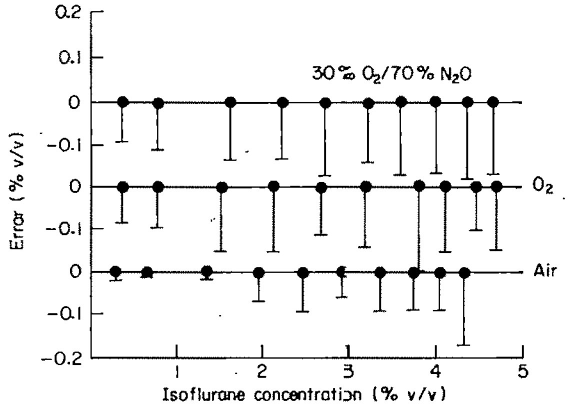

Fig. 11. Accuracy of measurement of isoflurane concentration in air, O_2 and 30% O_2/70% N_2O. The errors are shown by horizontal bars.

associated with the analysis of the volatile agents in air, O_2 and 30% O_2/70% N_2O is shown in Figures 9, 10 and 11. The errors were greater with enflurane than with the other two agents.

Zero and gain stability

The zero of both gas and volatile agent readings was unchanged after 18 hours of sampling air. After this period the calibration for N_2O and enflurane was unchanged, the CO_2 had increased from 6.0 to 6.2% and the O_2 had increased from 21 to 22%.

Response and delay times

These are shown in Table 2. The results agree with the manufacturer's specifications. When the instrument was tested with the standard sampling catheter and square wave changes in gas composition at simulated breathing frequencies from 5 to 60 cycles per minute, it was found that there was no attenuation of the CO_2 response throughout this range (Fig. 12). The O_2 response began to fall off above 35 breaths/minute but the halothane response was impaired above 15 breaths/minute. Substitution of a 5-cm long tube for the normal length sampling tube (Fig. 13) had little effect, which suggests that the attenuation of the response was associated with the longer instrumental response time with the anaesthetic vapour.

Effect of water vapour

The addition of water vapour to the gas and vapour mixtures investigated appeared to have no more effect on the measured gas concentrations than would have been predicted from its vapour pressure at 37°C. Condensation of water vapour within the sampling system did not appear to be a problem and the sample line occlusion alarm was not activated during the tests.

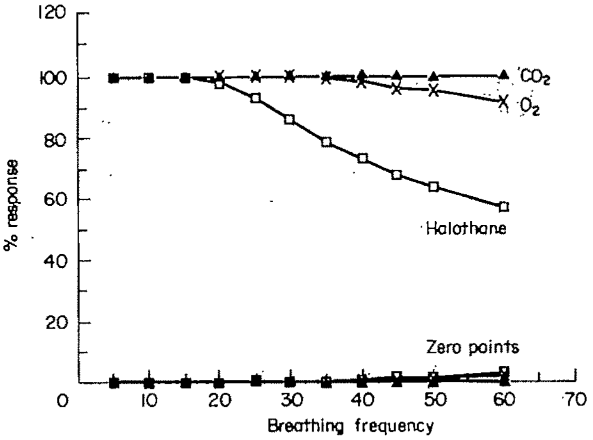

Fig. 12. Response of Capnomac to square wave changes, measured using Datex sampling tube.

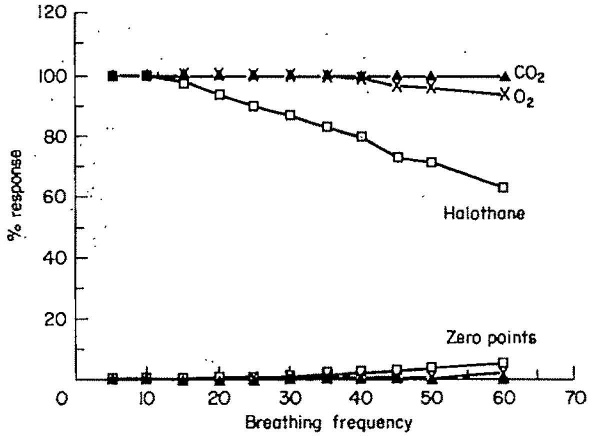

Fig. 13. Response of Capnomac to square wave changes, measured using 4 cm sampling tube.

Discussion

There has long been a need for a multigas and vapour analyser, capable of following breath-by-breath changes in the concentration of CO_2, O_2, N_2O and anaesthetic vapours. Until now the only analyser capable of making all these measurements simultaneously was the mass spectrometer. This instrument is complex, expensive, tends to drift, and may be unreliable after being contaminated by some of the propellants used in asthma inhalers.[7]

Dedicated mass spectrometers have been used in anaesthesia, but most instruments have been used in the multiplex mode so that samples from a number of operating theatres may be sampled in turn. This results not only in a delay in the transmission of the sample from the patient to the machine, but a sampling period which may be limited to 15 seconds in every 3 minutes if 12 operating theatres are being sampled by one machine. Although satisfactory infrared analysers for CO_2 have been available for many years, analysers for anaesthetic vapours have tended to have a slow response, and may be affected by water vapour or become inaccurate when used over a period of time.[8,9]

Paramagnetic O_2 analysers have also been available for some time, but the speed of response precluded breath-by-breath measurement.

The Capnomac utilises narrow wave band filters to increase the specificity of the instrument for CO_2 and N_2O, but cannot identify the anaesthetic vapours since these are measured with the same wave band. The rapidity of response to CO_2 and O_2 should be adequate for most paediatric and adult patients, but some inaccuracy must be expected at higher breathing frequencies with N_2O and the volatile agents.

The Capnomac has only been evaluated over a limited period under laboratory conditions. Nevertheless the results suggest that the instrument represents a significant advance in the monitoring of inspired and expired gases and vapours during anaesthesia.

Acknowledgment

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APPARATUS

Long-term performance of Tec vaporizers

Basis for a rational maintenance policy

K. B. CARTER, W. M. GRAY, R. RAILTON AND W. RICHARDSON

Summary

We reviewed the maintenance records of Tec vaporizers which had been in clinical use for up to 4 years. Tec 4s and Enfluratec 3s were found to be extremely reliable, but Fluotec 3s suffered progressively from mechanical and calibration problems. Their most recurrent fault was sticking valves caused probably by thymol crystallising on the valve faces. This fault did not occur with Fluotec 4s, which are designed to prevent liquid agent reaching the valve surfaces. We found, in a study of the effects of thymol accumulation, that only occasional draining of a Fluotec vaporizer is required to keep thymol concentration below the level at which its output is reduced. We conclude that, if regular field calibration checks are carried out as a safety measure, the service interval for Tec vaporizers could be extended beyond Ohmeda's present recommendation of one year.

Key words

Equipment; vaporizers.

Anaesthetic vaporizers have been closely scrutinised over the years. The impression that could be gained from the literature is that they are prone to failure and require regular care and attention from users and manufacturers.[1–7] However, it is some time since the reliability of vaporizers was assessed systematically.[8] There have been major improvements in design since then,[9] in particular in the Tec 3 and Tec 4 ranges (manufactured by Ohmeda Ltd) which have emerged as the most popular models in the UK.

One factor which may affect the performance of vaporizers is the accumulation of contaminants and stabilisers.[10] This has led to recommendations by manufacturers regularly to drain them.[11,12] In this study we present data on the long-term performance of Tec 3 and Tec 4 vaporizers in clinical use. We report the results of a theoretical study on the effects of thymol build up in Fluotec models. Finally, we make recommendations with regard to maintenance.

Maintenance policy

All vaporizers in the West of Scotland are given 6-monthly calibration checks by medical physics staff. Those that fail these tests are returned to Ohmeda; apart from this, there is no uniform policy for returning vaporizers. Some are sent annually (as recommended by Ohmeda), some every 2 years and others at longer intervals. Vaporizers with sticking valves are attended to by medical physics staff who remove the valve cover and clean the valve surfaces.

Ohmeda recommend that Fluotec vaporizers should be drained 'at intervals not exceeding 2 weeks ... when the agent level is low',but that 'less frequent intervals' may be used for Enfluratecs and Isotecs. Implementation of this policy is the responsibility of theatre staff.

Vaporizer testing

Calibration procedure

A Riken Model 18 interferometer is used to measure vaporizer output either in the operating theatre or a hospital laboratory. All vaporizers are allowed to equilibrate to room temperature before calibration. Oxygen at a flow of 5 litres/minute is passed through the vaporizer under test which is initially set to the 'off' position (7 litres/minute is used for Enfluratec 5% models). Its output is fed to a stainless steel mixing chamber and then to a scavenging system. Samples of gas are drawn from the mixing chamber through a side opening to the interferometer using a hand aspiration bulb. Readings are made continuously until stability is reached, usually after 30 seconds. The flow is then switched off and a final measurement is recorded under 'no flow conditions'. This procedure is repeated

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Table 1. Acceptance limits for Tec vaporizers.

Vaporizer setting % concentration	Acceptance limits % concentration
0	0
0.5	± 0.2
1.0	± 0.25
2.0	± 0.4
3.0	± 0.5
4.0	± 0.65
5.0	± 0.8

with the other dial settings on the vaporizer and takes approximately 10 minutes to complete.

Criteria for acceptance

We have decided, in the absence of any published data from Ohmeda on accuracy of their vaporizers, that the output is acceptable if it is within 10% of the dial setting. To determine whether a vaporizer is within these limits, the errors in measurement must be added to these limits.

Absolute accuracy of an interferometer is difficult to assess as it relies ultimately on the knowledge of refractive index of the vapour being measured. Values reported for the refractive index of anaesthetic vapours are inconsistent.[13] Also errors are introduced by the operator of the instrument in estimating fringe position. Taken together, we estimate these errors as ± 0.1% concentration ± 3.5% of reading. Hence our acceptance limits for a vaporizer are ± 0.1% concentration ± 13.5% of reading. Table 1 shows the limits for different dial settings.

We stipulate one further requirement for the linearity of output. The output must change by not less than 0.6% concentration and not more than 1.4% concentration when the dial setting on the vaporizer is moved by 1% concentration. This applies over the entire range of settings.

Methods

Long-term performance

We examined the maintenance records of Fluotec 3s and 4s and Enfluratec 3s and 4s from two units within Greater Glasgow Health Board to determine the types and frequencies of faults and to see whether the performance of vaporizers changed with time.

Dependence of thymol concentration on halothane usage and draining policy

Fluothane (ICI) was used in Fluotec vaporizers throughout the period of the study and examination of the records of three hospitals showed that the average usage rate was between 60 and 125 ml/week/vaporizer and the maximum rate in a single vaporizer was 250 ml/week. We assumed a 'worst case' usage rate of 500 ml/week in estimating thymol accumulation. Two situations were considered: no liquid is drained from the vaporizer; 50 ml drained from the vaporizer at the end of each 2-week period when the level shown in the sight glass is at midpoint.

Case A. No draining

Continued use of a Fluotec vaporizer without its being drained will cause the mass of thymol in its sump to rise by 0.187 g for each litre of Fluothane added. The concentration of thymol in the sump C_s, can be determined if the total volume of Fluotec added V_a and the volume of agent in the sump V_s are known.

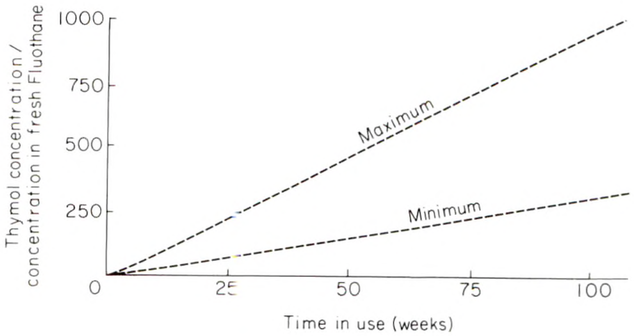

Fig. 1. Accumulation of thymol in a Fluotec vaporizer which is used for 2 years without draining. 500 ml halothane consumed per week.

$$C_s = \frac{V_a}{V_s} \text{ units.}$$

where 1 unit = the concentration of thymol in fresh Fluothane.

After a Fluotec 3 has been filled[9] to the 'full' mark, V_s is 150 ml and thymol concentration will be $\frac{V_a}{150}$ units.

When the anaesthetic agent reaches[9] its lowest level V_s is 50 ml and thymol concentration will be $\frac{V_a}{50}$ units.

Figure 1 shows that for a vaporizer consuming 500 ml of Fluothane per week, the maximum thymol concentration (measured when $V_s = 50$) and the minimum thymol concentration (when $V_s = 150$) both increase linearly with time.

Case B. Regular draining

Draining a Fluotec vaporizer removes only some of the thymol since a proportion is left in the 50 ml of agent retained in the wicks and sump after draining.[9] This results in accumulation of thymol in the vaporizer at a rate which depends on the usage of Fluothane, the amount of agent drained and the frequency of draining.

Consider for example, a Fluotec vaporizing 500 ml of liquid Fluothane per week, drained of 50 ml to the 'minimum level' every fortnight. The maximum and minimum thymol concentrations approach limiting values ($C_{\text{max.lim}}$, $C_{\text{min.lim}}$) exponentially as Figure 2 illustrates. Actual concentrations vary, increasing as halothane vaporizes and decreasing each time the vaporizer is refilled. This effect is shown for two cycles of filling and draining during weeks 4–8.

$C_{\text{max.lim}}$ will be reached when the amount of thymol removed by draining volume V_d of agent equals the amount of thymol in V_c, the volume of fresh Fluothane added during the cycle.

$$\text{i.e. } V_d \times C_d = V_c \times 1$$

$$\therefore C_d = \frac{V_c}{V_d} \text{ units}$$

where C_d = thymol concentration in V_d.

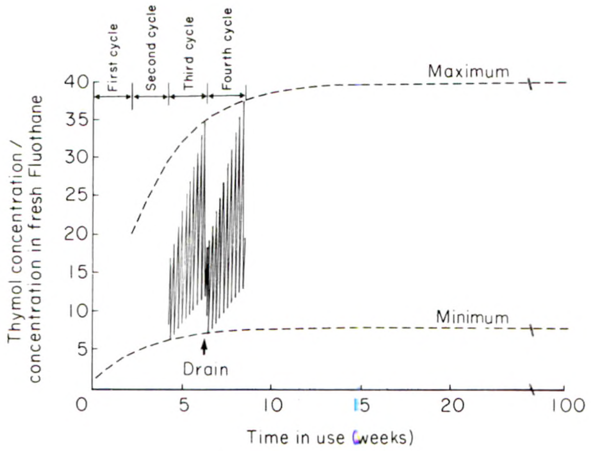

Fig. 2. Accumulation of thymol in a Fluotec vaporizer drained every 2 weeks of 50 ml halothane. 500 ml halothane consumed per week.

Table 2. Vaporizer faults during 4 years of use.

	Period (months)			
	0–12	12–24	24–36	36–48
Fluotec 3				
Total vaporizers	80	70	54	32
Faults				
Calibration	5 (6%)	6 (9%)	4 (7%)	5 (16%)
Sticking	9 (11%)	12 (17%)	5 (9%)	3 (9%)
Mechanical	3 (4%)	4 (6%)	3 (6%)	1 (3%)
Total faults	17 (21%)	22 (32%)	12 (22%)	9 (28%)
Enfluratec 3				
Total vaporizers	70	65	45	34
Faults				
Calibration	2 (3%)	4 (6%)	0	2 (6%)
Sticking	0	0	0	0
Mechanical	0	2 (3%)	3 (7%)	1 (3%)
Total faults	2 (3%)	6 (9%)	3 (7%)	3 (9%)
Fluotec 4				
Total vaporizers	32	26	24	16
Faults				
Calibration	0	0	0	0
Sticking	0	0	0	0
Mechanical	3 (9%)	4 (15%)	2 (8%)	2 (13%)
Total faults	3 (9%)	4 (15%)	2 (8%)	2 (13%)
Enfluratec 4				
Total vaporizers	11	9	8	55
Faults				
Calibration	0	0	0	0
Sticking	0	0	0	0
Mechanical	0	0	0	1 (20%)
Total faults	0	0	0	1 (20%)

$C_{max.lim}$ will occur immediately before the last refill when $V_s = 50$ ml, since the vaporizer is drained when $V_s = (V_d + 50)$ ml.

$$\text{Hence } C_{max.lim} = \frac{(V_d + 50) \times C_d - 100}{50} \text{ units} \ldots \qquad \text{eqn (1)}$$

This equation takes account of the 100 units of thymol added at the last filling.

$C_{min.lim}$, occurs immediately after draining and refilling.

$$C_{min.lim} = \frac{(50 \times C_d) + 100}{150} \text{ units}$$

In the above example, when the vaporizer is drained fortnightly, application of the above equations give,

$$C_d = \frac{1050}{50} = 21 \text{ units}$$

$$C_{max.lim} = \frac{(50 + 50) \times 21 - 100}{50} = 40 \text{ units}$$

$$C_{min.lim} = \frac{(50 \times 21) + 100}{150} = 7.67 \text{ units}$$

Results

Long-term performance

Table 2 summarises the maintenance records of all vaporizers studied. Calibration faults which occurred in Fluotec 3s and Enfluratecs 3s were usually as a result of output decreasing just below our calibration limit, although three of the Fluotec 3s failed because they delivered up to 130% of their dial setting. There were no calibration failures in Tec 4s. Four of the mechanical faults with the Fluotec 4s were because of leaking seals in their keyed fillers.

Dependence of thymol concentration on halothane usage and draining policy

Maximum and minimum thymol concentrations increase uniformly over the 2-year period, when no liquid is drained from a vaporizer (Case A, see Fig. 1). With draining (Case B) the maximum and minimum values of thymol concentration increase rapidly at first, but the rate of increase falls off until the values become almost steady after about 15 weeks. The maximum concentration is about 40 times the concentration in fresh Fluothane. The thymol concentration fluctuates between the minimum and maximum values as the result of the use of halothane and periodic refilling. This is shown in Figure 2.

Discussion

Long-term performance

A greater incidence of faults was found in the Fluotec 3s compared to all other vaporizer types. This was principally the result of valve sticking which accounted for most of the faults and was probably associated with the crystallisation of thymol as discussed below. Deposits of thymol on the valve may also alter the calibration of Fluotec 3s.

It was interesting to note that since 1984 there has been a significant reduction in sticking and calibration faults in Ohmeda's Fluotec 3s. Pinpointing the reasons for this was difficult: some of these vaporizers were stripped and cleaned on a regular basis as a preventative measure; the pattern of usage of Fluotecs was changing as more Enfluratec vaporizers became available.

All Fluotec 4s in this study were mounted on Ohmeda anaesthetic machines fitted with Selectatec backbars to accommodate two vaporizers. They were seldom removed from their machine which probably accounts for no recorded instances of the locking mechanism failing.[6]

Drainage of vaporizers

All pharmaceutical products contain contaminants that are unavoidable byproducts of the manufacturing process and halothane is no exception; it has at least 15 impurities.[14] These are harmless to patients in anaesthetic mixtures of halothane.[15] Furthermore, it appears that no significant concentration of impurities in vaporizers occurs as halothane is consumed.[16] Thus, it would seem that it is unnecessary to drain halothane vaporizers to remove accumulated contaminants.

Halothane also contains thymol, which is not a contaminant but a stabiliser introduced at a concentration of 0.01% w/w. Thymol has very low volatility,[17] and accumulates in vaporizers by fractional distillation as halothane is consumed.[18] In addition, oxidized thymol can accumulate and impart a yellowish brown colour to the halothane residue.[18] The accumulation of thymol could, in principle, lead to undesirable consequences. First, could toxic concentrations of thymol reach the patient? Thymol is present in many commercial inhalants. At high concentrations it produces a moderate increase of mucous secretion of the respiratory tract.[19] However, even if a vaporizer contained halothane almost saturated with thymol, the maximum vapour pressure that could be delivered to the patient would be about one-tenth of the vapour pressure of pure thymol. Therefore we agree with the previous workers that thymol accumulation does not represent a direct risk to the patient.[10,18] Likewise, the oxidation products of thymol are nonvolatile, and do not represent a risk to the patient.[18]

The second effect of thymol accumulation is a reduction of the output of the vaporizer as a result of halothane dilution. The study undertaken by Gray[20] shows that thymol concentration in a Fluotec 3 vaporizer has to increase by a factor of more than 600 before the output is reduced by 5%. Such a reduction would have little clinical significance.

Third, thymol also appears to be implicated in the sticking of vaporizer valves. Thymol will be deposited when halothane evaporates if a vaporizer is tilted and the liquid agent comes into contact with the valve surfaces. This will tend to produce sticking and will be more pronounced with higher concentrations of thymol. This as our findings show, applies only to the Fluotec 3 and not the Fluotec 4 which is designed to avoid spillage.

Even under conditions of heavy halothane usage, draining of 50 ml every fortnight keeps the thymol concentration at less than 50 times the concentration in fresh Fluothane (Fig. 2). In fact, the 'times 600 level' would not be exceeded if 50 ml were drained every 6 months from a half full vaporizer. The only reason to drain enflurane or isoflurane vaporizers would be to dilute any accumulated impurities. There is no evidence that suggests any accumulation occurs apart from a report of impurities produced in some Ohio vaporizers.[21] Indeed, one vaporizer manufacturer, Draeger, states that it is not necessary to drain these agents.[22] Ohmeda's recommendation that Enfluratecs and Isotecs should be drained at intervals 'less frequent than a fortnight' requires clarification.[23]

Conclusions

Our results suggest that, with the exception of Fluotec 3s, Tec 3 and 4 vaporizers are very reliable instruments. We recommend as a safety measure, that if they are used for long periods their calibration should be checked at least once a year. Seals must be replaced when those fitted with keyed fillers develop leaks.[24] Fluotec 3s however have the recurring problem of valve sticking, a fault that can be rectified easily at the hospital, but only by competent staff. Tinkering creates hazards.[24] The theory behind vaporizers draining has been poorly understood and erratic in implementation. Perhaps this aspect of maintenance could be regularised by synchronising it with maintenance of the anaesthetic machine.

To have Tec vaporizers returned to the manufacturer each year for a service is expensive; regular field calibration checks can provide the necessary safety assurance to allow them to continue in service beyond Ohmeda's currently recommended servicing interval.

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APPARATUS

Dependence of the output of a halothane vaporizer on thymol concentration

W. M. GRAY

Summary

The effect of thymol accumulation inside a Fluotec 3 vaporizer on the concentration of halothane delivered by the vaporizer was investigated. The vaporizer output was reduced progressively as the thymol concentration increased, but the reduction was less than that predicted by Raoult's Law. A reduction of 5% in output required an increase in thymol concentration of a factor of 650 compared to the concentration in fresh halothane, while a reduction of 10% required a 1100-fold increase in thymol concentration. The equilibration of the thymol from the wicks throughout the vaporizing chamber was very slow after the vaporizer was drained and filled with fresh halothane; the half-time was 2.7 days.

Key words

Anaesthetics; volatile.
Equipment; vaporizers.

Fluothane (ICI) contains 0.01% w/w thymol which acts as a stabiliser and prevents oxidation of the halothane. Pure thymol is a solid at room temperature and its vapour pressure is very low.[1] It therefore accumulates in vaporizers by fractional distillation as halothane is vaporized.[2] This accumulation could have several undesirable consequences.[3] One is a reduction of the halothane concentration delivered by the vaporizer, as a result of a decrease of the vapour pressure of halothane within the vaporizing chamber (see the Appendix). The purpose of this study was to determine the relation between thymol concentration and vaporizer output.

Methods

Thymol determinations

Thymol concentrations were measured by means of a Perkin-Elmer Sigma 3B gas chromatograph equipped with a thermal conductivity detector. A glass column (2 m × 4 mm internal diameter) packed with 80–100 mesh Chromosorb WHP coated with 10% silicone OV101 was used at a temperature of 200°C. The carrier gas was 80 litres/minute helium; the sample was introduced by flash vaporization of 1 μlitre at 250°C, and the detector temperature was 250°C. A Hewlett-Packard HP 3390A reporting integrator was used to calculate concentrations on the basis of peak areas. The retention times for halothane and thymol were 0.6 minute and 1.8 minute respectively. Preliminary tests showed that the detector's response to thymol was linear over the concentration range of interest. It is convenient to express thymol concentration as a multiple of the concentration in fresh Fluothane, which is 0.1869 g/litre (0.01% w/w). This concentration will be referred to as a 'unit'.

For routine thymol determinations, the detector was calibrated with at least two samples of a 500 unit standard, and at least two samples of the solution under test were analysed. In addition to the determinations described below, the concentration of thymol in a solution of halothane saturated with thymol was measured.

Dependence of vaporizer output on thymol concentration

The halothane concentrations delivered by a Fluotec 3 vaporizer (Ohmeda) for a carrier gas flow of 5 litres/minute oxygen were measured with a Riken portable interferometer, whose calibration had been checked by an accurate gas chromatographic method.[4] Vaporizer settings of 0.5, 1, 2, 3, 4 and 5% were used. Measurements were made with the vaporizer charged with fresh Fluothane, and these were taken as reference values. The vaporizer was then drained and charged with halothane almost saturated with thymol. The density of the halothane solution was determined by draining and weighing 10 ml, when the

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thymol had equilibrated throughout the vaporizing space (as indicated by stability of the thymol concentration in serial samples taken from the sump). The vaporizer output was then measured with the interferometer. Knowledge of the molar masses of thymol and halothane (150.22 g/mol and 197.39 g/mol respectively) allowed their mole fractions to be calculated from the measured density and thymol concentration. The ratio of vaporizer output to the reference output at each setting was calculated and the mean ratio determined.

Other thymol concentrations were obtained by draining appropriate volumes of halothane and filling with either fresh Fluothane or Fluothane that contained extra thymol. The above procedure was repeated in each case when the thymol concentration had stabilised.

Results

Concentration of thymol in a saturated solution

The concentration of thymol in a solution of halothane saturated with thymol was 3.05 × 10^3 units (0.569 g/litre).

Time for equilibration of thymol concentration within vaporizer

Equilibration was achieved by 2 days (no samples were taken earlier) when the thymol concentration within the vaporizer was increased. However, when the concentration was reduced, it took over a week for equilibration to occur; the approach to equilibrium was approximately exponential, with a half-time of 2.7 days (two separate series of measurements yielded half-times of 2.6 days and 2.8 days).

Dependence of vaporizer output on thymol concentration

The variation in vaporizer output with thymol concentration is shown in Figure 1. The broken line in the figure corresponds to Raoult's Law (equation (1) in the Appendix) with the thymol content expressed as a concentration rather than a mole fraction. The measured halothane concentrations became progressively greater than those predicted by Raoult's Law as the thymol concentration increased; at the maximum thymol concentration investigated (2670 units), the halothane concentration was 66% higher than the Raoult's Law value.

Discussion

Modern anaesthetic vaporizers produce a particular concentration of volatile agent by mixing appropriate proportions of fresh carrier gas and carrier gas saturated with the volatile agent. Thus, a reduction in the vapour pressure of the volatile agent in the vaporizing chamber will be reflected in a proportional reduction in the concentration delivered by the vaporizer. In halothane vaporizers, thymol accumulates by fractional distillation as halothane is vaporized and removed by the carrier gas, and the resultant dilution of the liquid halothane by the thymol causes a reduction in the vapour pressure of halothane in the vaporizing chamber and a consequent reduction in output. The mechanism by which the vapour pressure of halothane is reduced by the presence of thymol is described more fully in the Appendix.

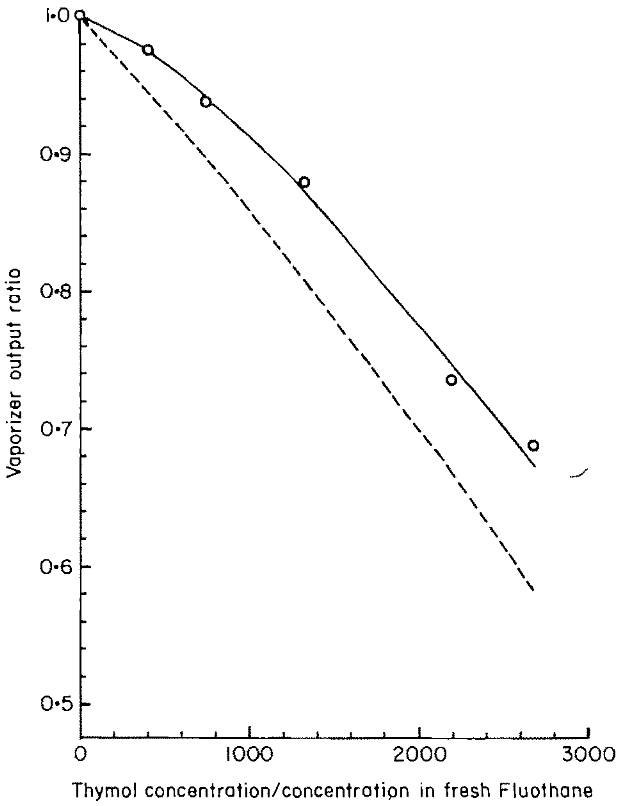

Fig. 1. Effect of different concentrations of thymol in halothane on the output of a Fluotec 3 vaporizer. The terms used in the figure are described in the text. O, measured values; ——, smooth curve through measured values (drawn by eye); ----, Raoult's Law prediction

The reduction of the vapour pressure of a solvent by a solute is in some cases accurately described by Raoult's Law and is discussed in the Appendix. However, this study has shown that the reduction in vaporizer output is less than that predicted by Raoult's Law. The law was derived empirically for mixtures of two closely related liquids, such as benzene and toluene,[5] so it is not too surprising that it does not provide an accurate description of the behaviour of a solution of solid thymol in liquid halothane. It can be seen from Figure 1 that the thymol concentration has to increase by a factor of 650 before the vaporizer output is reduced by 5%, and by a factor of 1100 before the output is reduced by 10%.

One unexpected finding was the length of time it took for thymol in the wicks to equilibrate throughout the vaporizing chamber after the vaporizer was drained and filled with fresh Fluothane; the half-time for this process was 2.7 days. This long equilibration time implies that thymol diffuses very slowly out of the wicks. However, the reverse process of equilibration from an initially high concentration in the sump was much quicker and was complete within 2 days. The reason for this difference is not clear.

The long equilibration time for the movement of thymol from the wicks to the sump suggests that, for a normal pattern of vaporizer use, the concentration of thymol in the wicks will be continuously greater than that in the sump. This has two interesting consequences. The first is that, as most of the halothane carried from the vaporizer by the carrier gas is picked up in its transit past the wicks, the reduction in vaporizer output will be greater than would be produced by the same amount of thymol evenly distributed throughout the vaporizing chamber. The second consequence is that, when the vaporizer is drained, less thymol will be removed than would be the case if the thymol were distributed evenly; thus the average concentration of thymol in the vaporizing chamber at any time will be greater than the nominal concentration obtained from a calculation based on the previous pattern of halothane usage and draining but assuming uniform thymol distribution. Both of the above effects will act together to produce a greater reduction in output than would be predicted from Figure 1 on the basis of a calculated nominal concentration of thymol.

The significance of the present findings for the formulation of a suitable draining policy for halothane vaporizers is discussed in the following paper.[3]

Appendix

Lowering of the vapour pressure of a solvent by a solute

The vapour pressure of a pure liquid is the pressure exerted by its vapour when it is in equilibrium with the liquid, that is when the number of molecules condensing in unit time is equal to the number evaporating in unit time. The presence of solute molecules reduces the concentration of solvent molecules in the liquid phase and also the number of solvent molecules evaporating in unit time. Equilibrium between solvent vapour and liquid will now be achieved at a lower pressure in the vapour phase and so the presence of the solute causes a reduction in vapour pressure of the solvent.

When the solvent and solute are chemically similar the reduction in vapour pressure is accurately described by *Raoult's Law*,[5] which states that the vapour pressure, P_A, of the solvent equals the vapour pressure, P_A^*, of the pure solvent multiplied by its mole fraction, x_A,

$$P_A = x_A P_A^*$$

If the mole fraction of the solute is x_B, then $x_A = 1 - x_B$, and the above equation can be written

$$\frac{P_A}{P_A^*} = 1 - x_B \qquad \text{eqn (1)}$$

Raoult's Law is an empirical result and, while some mixtures follow it closely, others show marked departures from it.[5]

In the present study, component A is halothane and component B thymol, and the results of the study allow the behaviour of this mixture to be compared with that predicted by Raoult's Law.

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Anaesthesia, 1988, Volume 43, pages 1050–1051

Forum

Intravenous fluids in minor gynaecological surgery. Their effect on postoperative morbidity

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Summary

Postoperative morbidity was assessed in 100 patients who underwent minor gynaecological procedures. Fifty patients received intra-operative crystalloid (1000 ml compound sodium lactate solution) and the remaining fifty none. Identical short-acting intravenous anaesthetic techniques were used in both groups. There was no statistically significant difference between the groups in symptoms of nausea, vomiting, headache and drowsiness within the first 6 hours after operation. Patients who received intra-operative fluids exhibited a decreased incidence of dizziness within the first 6 hours and a decreased incidence of nausea when questioned at 3 days compared with those who did not receive any fluid; the difference was statistically significant.

Key words

Complications; postoperative.
Fluid balance; intra-operative, crystalloid.

Dehydration, secondary to deprivation of oral fluids before routine surgery, has been alleged to cause postoperative symptoms of dizziness, headache and drowsniness.[1] In many countries all patients who undergo surgery receive intravenous fluids, irrespective of the length or type of operation. In the United Kingdom it was not previously routine practice to give replacement fluid therapy, except to patients who undergo major surgical procedures. Keane and Murray showed that patients undergoing minor surgery recovered more quickly from the effects of surgery and anaesthesia if they received intra-operative crystalloids compared with those who did not receive fluid replacement.[1] The present study was undertaken to evaluate the effect of intra-operative intravenous fluid therapy on postoperative morbidity in patients undergoing short gynaecological procedures.

Method

The study was reviewed and approved by the ethics committee of the hospital and informed consent was obtained from the patients. One hundred healthy women of ASA grades 1 or 2, aged 18–50 years, who were to undergo minor gynaecological surgery, such as diathermy to cervix, dilatation and curettage and termination of pregnancy, were allocated randomly into two groups. Patients in Group 1 were allocated to receive 1000 ml of compound sodium lactate solution intra-operatively; those in Group 2 received no intra-operative fluids.

All patients were premedicated with oral temazepam 20 mg, administered one hour before operation. An 18-G cannula was placed in a superficial vein in the forearm, and alfentanil 3 μg/kg was given intravenously before induction of anaesthesia with intravenous propofol 2 mg/kg. Anaesthesia was maintained with 66% nitrous oxide in oxygen administered through a Bain system, with incremental doses of alfentanil and propofol. The maximum dose of alfentanil was limited to 10 μg/kg to minimise the incidence of respiratory depression in these spontaneously breathing patients. The remainder of the calculated dose of alfentanil was given in three equal increments intra-operatively. Propofol was given at induction and in 20-mg increments throughout the operation as necessary to keep the patient anaesthetised. The total dose of propofol was not restricted. Spontaneous respiration was maintained throughout and tracheal intubation was not required.

The age and weight of the patient, the type of operation and induction and total doses of propofol and alfentanil used were recorded. The duration of anaesthesia, defined as the time from the induction of anaesthesia with propofol to the time the nitrous oxide was stopped, was also recorded. Syntocinon 10 units was given intravenously to patients who underwent termination of pregnancy.

Two questionnaires were used to assess postoperative morbidity. The first, completed at 6 hours after operation, was designed to establish the presence of nausea, vomiting, dizziness, drowsiness, headache, thirst and urinary retention, and required a simple yes/no response. The second was completed on the third day after operation and asked about the presence of nausea, headache, dizziness and appetite; further questions designed to assess the patient's general well-being, vigour and their present feelings compared with their state before operation were also included. Patients were asked whether the injection site was painful, and whether they had found the infusion inconvenient.

Data were analysed for statistical significance, using Student's t-test and Chi-squared analysis as appropriate. Results were considered significant at a probability of $p < 0.05$.

Results

The two groups were similar in age and weight. Twenty patients in each group received syntocinon. There was no statistically significant difference between the groups in the duration of anaesthesia or the total doses of alfentanil and propofol given (Table 1). There was no statistically significant difference between the groups in the incidence of

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Table 1. Patient details, surgery duration and drug doses. Values expressed as mean (SD).

	Group 1 (crystalloid given) $n = 50$	Group 2 (no crystalloid given) $n = 50$	Significance
Age, years	32.7 (11.4)	32.0 (10.2)	NS
Weight, kg	64.1 (11.5)	63.4 (10.7)	NS
Duration of surgery, minutes	8.0 (3.5)	7.6 (3.3)	NS
Induction dose of propofol, mg	117 (17.5)	112 (16.7)	NS
Total dose of propofol, mg	164 (25.8)	162 (30.1)	NS
Total dose of alfentanil, mg	598 (96.8)	592 (108)	NS

NS, not significant.

nausea, vomiting, headache or drowsiness in the first 6 hours (Table 2). The incidence of dizziness in the first 6 hours was 10% and 28% in Groups 1 and 2 respectively and this was statistically significant (p = 0.04). Eight patients in Group 2 experienced nausea after the initial recovery phase, whereas none of the Group 1 patients were nauseated at this time; the difference was statistically significant (p = 0.01). No statistically significant difference was found with any of the other symptoms (Table 3). Patients had either several symptoms or none at all. Thirty-three of the 100 patients complained of headache and 27 of drowsiness.

Table 2. Results of the first questionnaire completed at 6 hours.

	Group 1 (crystalloid given) $n = 50$	Group 2 (no crystalloid given) $n = 50$	Significance
Nausea	6 (12%)	11 (22%)	NS
Vomit	1 (2%)	1 (2%)	NS
Headache	14 (28%)	19 (38%)	NS
Drowsy	11 (22%)	16 (32%)	NS
Dizzy	5 (10%)	14 (28%)	p = 0.04
No symptoms	25 (50%)	16 (32%)	NS

NS, Not significant.

Table 3. Results of the second questionnaire completed at 3 days.

	Group 1 (crystalloid given) $n = 50$	Group 2 (no crystalloid given) $n = 50$	Significance
Nausea	0 (0%)	8 (16%)	p = 0.01
Headache	6 (12%)	7 (14%)	NS
Sleepiness	9 (18%)	12 (24%)	NS
Dizziness	6 (12%)	5 (10%)	NS
Feeling lacking in energy	19 (38%)	21 (42%)	NS
Feeling as well as before operation	33 (66%)	34 (68%)	NS
No symptoms	36 (72%)	33 (66%)	NS

NS, Not significant.

Discussion

Many patients suffer some morbidity after minor surgical procedures, much of which is unrecorded and unrecognised, but may nonetheless inconvenience the patients to a greater or lesser extent. Fahy and Marshall studied postanaesthetic morbidity in outpatients and showed a high incidence (45%) of somatic disturbances after general anaesthesia for minor procedures.[2] They concluded that the occurrence and severity of the symptoms depended on the length of the operation. Drowsiness was the commonest complaint, followed by headache, malaise and nausea. Many patients presenting for anaesthesia and surgery have been starved for 12–18 hours and their postoperative morbidity may be attributable to general dehydration.

There has been considerable debate over the last 30 years about the use of peri-operative intravenous fluid.[3–5] Most studies have been of patients undergoing major surgery and little work has been published on the possible effects of intravenous fluids during minor surgery. Keane and Murray showed that patients undergoing minor surgical procedures who received 2 litres of intravenous crystalloids had decreased postoperative morbidity.[1] Their study included a much wider variation in the type of operation and the duration of surgery (10–45 minutes, mean 18 minutes) than is described here.

Several factors contribute to postoperative dehydration, and include lack of oral fluids pre-operatively, insensible losses peri-operatively, and intra-operative blood and 'third space' losses. Postoperative dehydration is further aggravated by a low oral intake immediately after surgery. A quantitative assessment of the degree of dehydration in patients presenting for minor surgery is difficult. The patients in this study had been starved for about 12 hours and so presented with a deficit of around 1000 ml of fluid which would cause a moderate decrease in both extracellular and intracellular fluid volumes.[6,7]

Could this dehydration account for the postoperative symptoms of nausea, drowsiness and headache? The results of this study do show that even in these very short surgical procedures the administration of peri-operative intravenous fluid does reduce the incidence of immediate postoperative dizziness. There was no statistically significant difference in the other symptoms studied possibly because the patients were undergoing surgery of very short duration (mean anaesthetic time of 7.8 minutes) and the anaesthetic was tailored to fit the length of the operation; the patients were fully awake, sitting up and talking almost immediately after the end of the procedure. The patients were allowed to eat and drink immediately they returned to the ward and all had had a drink within 6 hours. The increased incidence of nausea at 3 days is very interesting but difficult to explain. Any residual dehydration should have corrected itself by this stage.

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'Fruit-flavoured' mask for isoflurane induction in children

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Summary

The effect of disguising the odour of isoflurane with fruit flavouring, upon the quality of inhalational induction, was studied in 41 children aged 3–10 years in a double-blind, randomised trial. Facemasks were either lightly coated with fruit extract or moistened with water so that their appearance was identical to children, anaesthetist and observer. Children allocated to receive fruit flavouring were significantly quieter than the placebo group, but their degree of movement during induction was unchanged. The incidence of respiratory complications including breath-holding, laryngospasm and coughing was similar in both groups. Overall impression of the quality of induction as assessed by the anaesthetist showed no difference between the groups. This simple, cheap modification of inhalational induction warrants further appraisal while the case for disguising the odour of isoflurane remains unproven.

Key words

Anaesthesia; paediatric, outpatient.
Anaesthetics volatile; isoflurane, odour.

Inhalational induction of anaesthesia can be an emotionally traumatic experience for children that results in irrational long-term fears of future anaesthesia.[1] Often the pungent odour of the volatile agent is cited as the most unpleasant aspect of this procedure.[2]

Halothane remains the most commonly used vapour for inhalational induction, but the reports of halothane hepatitis in children on repeated exposure[3] have led to an increasing usage of isoflurane, a fluorinated ether. The physical characteristics of isoflurane are also attractive which suggest it should produce a more rapid induction than halothane. However, it is generally regarded as an irritant;[4] its odour is disliked by patients, with a high incidence of respiratory complications during induction.[5] Enflurane differs from its isomer, isoflurane, in that children appear not to have a preference between the smell of enflurane and halothane.[6] In addition, enflurane induction does not result in the high incidence of coughing and laryngospasm that occurs during isoflurane induction.[5] Consequently there seems little to be gained from disguising the odour of enflurane.

Gregory[7] refers to the addition of 'fruit flavouring lightly coating the inside of the anaesthetic mask', to obscure the odour of the volatile agent. Smith[8] suggests in his textbook that 'masks can be decorated with designs and colours, and the smell of rubber (and anaesthetics) can be disguised by a drop of perfume or fruit extract placed either on the mask or under the children's nose'. This minor modification of inhalational induction appears to be worthwhile on empirical grounds, although no formal studies have been reported in the literature to assess its value. We have attempted, therefore, to improve the quality of induction with isoflurane by disguising its odour with fruit flavouring placed on the facemask.

The objectives of the study were to assess whether by disguising the odour of isoflurane, induction could be made more pleasant for the children, as well as produce fewer problems for the anaesthetist.

Methods

Forty-one unpremedicated children, aged 3–10 years scheduled for routine day care minor general surgical or urological procedures were studied, after approval by the local District Ethics Committee. Full informed consent was obtained from accompanying parents. The children were allocated randomly into two groups; Group A, to receive fruit flavouring ($n = 21$); Group B, not to receive fruit flavouring ($n = 20$). Children allergic to food colouring/flavouring or deemed atopic were to be excluded from the trial.

Routine pre-operative assessment was performed by a single anaesthetist who was responsible for administration of anaesthesia to all patients. Subsequently children were visited on the ward by one of two trained observers, and told that a special 'strawberry wind' would put them to sleep for their operation. The anxiety state of the children in the presence of one or both parents was categorised on a three-point scale. The children's anxiety levels were assessed again when the child entered the anaesthetic room. No parent was then present.

Those patients allocated randomly to receive strawberry flavouring (Supercook Ltd, Leeds) had the inside of their facemasks lightly coated with two drops of the fruit extract, while the remaining facemasks were merely moistened with water so that their appearance was identical. Anaesthetist and observer were unaware of all extraneous odours by smearing their surgical masks with strawberry flavouring.

Anaesthesia was induced with a T-piece or Bain system as appropriate, 66% nitrous oxide in oxygen and isoflurane.

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Table 1. Details of children. Values expressed as mean (SEM).

	Group A (n = 21)	Group B (n = 20)
Age, years	5.8 (0.3)	5.2 (0.4)
Weight, kg	20.5 (0.9)	17.4 (0.9)*
Males:females	16:5	16:4

* Significant at $p < 0.05$ unpaired Student's t-test

Table 2. Procedures performed.

	Group A (n = 21)	Group B (n = 20)
Circumcision	10	10
Inguinal hernia	5	2
Hydrocoele	1	2
Cystoscopy	1	4
Umbilical hernia	3	–
Dermoid cyst	1	–
Rectal biopsy	–	1
Tongue tie	–	1

Table 3. Assessment of children before induction.

	Group A (n = 21)	Group B (n = 20)
Pre-operative state		
Not anxious	14	7
Anxious, but cooperative	6	10
Very anxious, not cooperative	1	3
Pre-induction state		
Cooperative	16	9
Anxious	4	7
Struggling	1	4

The facemask was initially held 2–3 cm from the child's nose and mouth and then gently moved so as to lie directly on the face while the child was still conscious. The concentration of isoflurane was adjusted as clinically indicated to minimise airway complictions.

The observer noted the presence and severity of complications during induction, and quantified the degree of cooperation as assessed by movement and noise from the children in the first 2 minutes. Induction times (placement of facemask to loss of eyelash reflex) were also recorded. Finally the anaesthetist was asked to categorise his impression of the initial 2 minutes of induction pertaining to the first stage of anaesthesia.

Results were analysed by unpaired Student's t-test and Chi-squared analysis with Yates' correction as appropriate.

Results

There were no significant differences in the mean ages, and sex of the children between the two groups, although the weight of children in Group A was significantly greater than those in Group B (Table 1). No exclusions were encountered in the course of recruitment to the study.

Four of the children in Group A and six in Group B had previously been anaesthetised by an inhalational technique using halothane. A further two children in Group B had received an intravenous induction in the past. The various operative procedures performed were similar in both groups (Table 2).

Table 4. Induction times, minutes (SEM).

Group A	2.32 (0.10)
Group B	2.23 (0.10)

Table 5. Incidence and severity of complications.

	Group A (n = 21)	Group B (n = 20)
Coughing		
None	8	12
Mild, one or two coughs	4	3
Moderate, more than two coughs, not compromising gas exchange	4	3
Severe, coughing compromising gas exchange	5	2
Laryngospasm		
None	7	9
Mild, positive pressure not required	4	3
Moderate, positive pressure required	9	8
Severe, suxamethonium or intubation required	1	–
Salivation		
None	10	12
Slight	4	5
Moderate	5	3
Excessive	2	–
Breath-holding		
Yes	10	8
No	11	12

Chi-squared analysis of data showed no statistically significant differences between the groups.

Table 6. Observer assessment of induction (initial 2 minutes).

	Group A (n = 21)	Group B (n = 20)
Movement		
Lying still	9	10
Small movements	8	5
Pushing mask away	1	–
Wriggling trunk	1	1
Kicking and fighting	2	4
Noise		
Quiet	18*	10
Wimper	–	4
Crying	1	1
Screaming	2	5

* Significant at $p < 0.05$ Chi-squared analysis with Yates' correction.

Observer assessment of the children's pre-operative anxiety state, in the presence of parents on the ward, and pre-induction state in the anaesthetic room, showed no differences between the groups (Table 3). Mean induction times were similar (Table 4). The incidence of induction complications that included coughing, laryngospasm, salivation and breath-holding were the same in both groups (Table 5). Movement of children during induction did not differ between groups, although those that received fruit flavouring appeared to be significantly quieter (Table 6). Finally, the impression of the anaesthetist on the quality of induction during the first 2 minutes was similar in both groups (Table 7).

Discussion

The ideal inhalational induction of anaesthesia should be pleasant both for the patient and present minimal problems for the anaesthetist. The time of greatest importance for the child, is the interval from placement of the mask on the face, to the loss of consciousness. We have attempted to quantify the compliance of the children during this period

Table 7. Anaesthetists' assessment of induction (initial 2 minutes)

	Poor	Adequate	Good	Excellent
Group A ($n = 21$)	2	3	7	9
Group B ($n = 20$)	2	5	8	5

by objective assessment of their degree of cooperation, as defined by grading their movements and the amount of noise they made. We were unable to show any difference between the groups with regard to cooperation, but there was a significant reduction in the vocalisation of those who received fruit flavouring on their mask.

The anaesthetist's prime objective is to minimise complications for the patient while accomplishing a rapid and smooth induction. Our experience with isoflurane revealed no difference in the frequency of respiratory complications including breath-holding, coughing and laryngospasm between the two groups. None of these were considered to be life threatening but the incidence was unacceptably high, an observation which has also been made by other investigators.[5,9] Consequently disguising the pungent odour of isoflurane appears not to modify the incidence of these respiratory complications. It could be argued that our limited experience with the use of this agent may be responsible, and that the anaesthetist was on a learning curve.[10] However, if this hypothesis was correct a progressive reduction of the complications throughout the study would have been expected, which was clearly not the case.

It is possible that the present study design failed to reveal any major differences between the groups because of placebo response. The observer at the pre-operative assessment told all children in the study that they would receive fruit flavouring. Consequently the expectations of the children were high and most arrived in the anaesthetic room happy and contented. Possibly without any previous mention of fruit flavouring such a desirable situation would not have existed and a greater difference would have become apparent between groups.

Other investigators[11] have suggested 'aerosolising' fruit flavouring by passing the inhalational gas mixture through a small chamber containing the extract. However, the potential toxicity of the ingredients of fruit flavouring has been discussed[12] and direct aerosolisation would appear unnecessarily dangerous. Our method of simply applying small quantities of fruit extract directly to the facemask is easier and safer to use. Commercially produced scented paediatric masks are available but considerably more expensive than a bottle of fruit flavouring!

Other methods[13,14] have been suggested to minimise the fear and suspicion of young children during the inhalational induction of anaesthesia, but they usually require the purchase or construction of special apparatus. The addition of fruit flavouring to paediatric facemasks to camouflage the pungent odour of inhalational agents and improve young patients' acceptance is a small, simple and cheap modification of existing anaesthetic practice which deserves wider appraisal.

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The incidence of pruritus after epidural morphine

Epidural narcotics are used commonly for postoperative pain control. A variety of side effects, including pruritus, are associated with the use of epidural morphine.[1] We compared the incidence of pruritus after epidural morphine in patients who had undergone Caesarean section, and in patients who had undergone major abdominal cancer surgery.

Group A included 32 women who received 2.5–3.0 mg epidural morphine sulphate after Caesarean section. Group B included 45 male patients who received 5.0–10.0 mg epidural morphine sulphate after major abdominal cancer surgery. All patients were questioned about itching during the first 48 hours after surgery; only patients who were alert and orientated were included. Patients with other known causes of pruritus were excluded.

The results are summarised in Table 1.

Table 1.

Group	Surgery	n	Mean age	Dose	Incidence of pruritus
A (female)	Caesarean section	32	28	2.5–3.0 mg	20/32 (62.5%)
B (male)	Cancer surgery	45	52	5.0–10.0 mg	5/45 (11.1%)

The incidence of pruritus in the Caesarean section patients was much higher than in the patients who underwent cancer

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surgery.[2] The difference in this incidence may be related to age, sex, hormonal factors, dose of morphine or type of surgery. Further studies must be considered taking each factor into consideration.

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Accidental epidural injection of a large dose of morphine

Epidural morphine may lead to respiratory depression during treatment of acute pain.[1] However, there are not enough data concerning respiratory depression when epidural morphine is used in chronic pain management. We report a patient who received an accidental epidural injection of high-dose morphine during chronic pain treatment.

A 57-year-old woman complained of increasing pain 2 years after hysterectomy as a result of carcinoma corporis uteri and carcinoma coli accompanied by metastasis to the inguinal lymph nodes. She was admitted to the hospital for pain treatment. It was decided to treat the patient with epidural narcotics, because she was not pain-free with a daily dose of 160 mg morphine given subcutaneously. An epidural catheter was inserted in the $L_{3/4}$ interspace and, after the correct position of the catheter was verified with a test dose containing lignocaine and adrenaline, 10 ml of an 0.04% solution equivalent to 4 mg of morphine was injected twice a day. This dose rendered the patient pain free. Thirty minutes after the usual amount epidurally her respiratory rate decreased from 20 to 8 breaths/minute on the sixth day after insertion of the epidural catheter. Repeated doses of intravenous naloxone 0.1 mg were given immediately to antagonise the respiratory depression. Oxygen was administered by way of a nasal tube and a pulse oximeter employed to monitor arterial oxygen saturation. The patient was very drowsy and developed stiffness of her arms and legs; her respiratory rate further decreased to 4–6 breaths/minute. The patient could open her eyes and move her joints only with difficulty.

The symptoms gradually faded away without further treatment. Twelve hours after the last injection of morphine the respiratory rate increased above normal (20–24 breaths/minute), and 12 hours later the patient was fully awake. She could get up from bed and wash herself without problems. Blood pressure and heart rate remained normal throughout the entire observation period. Later it was found that the nurse who prepared the syringe had erroneously drawn up 10 ml from a 2% solution prepared for oral intake equivalent to 200 mg of morphine. The syringe had already been filled when it was handed over to the anaesthesiologist.

Surprisingly, 200 mg that contained preservatives instead of the prescribed 4 mg of preservative-free morphine accidentally injected into the epidural space produced neither apnoea nor a lethal respiratory depression and did not cause any definitive neurological damage to the patient. The preservatives contained in this solution were of alcoholic origin and may be held responsible for the temporary pathologic reactions of the central nervous system. Seven days later the patient was discharged from the hospital in a satisfactory condition.

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Reference

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Total parenteral nutrition and respiratory failure

We wish to draw attention to an incident encountered recently in which a patient who was receiving parenteral nutrition developed respiratory failure. The amino acid component was found to be an aetiological factor.

A 64-year-old, 50 kg woman was admitted with a past history of Crohn's disease (for which she required a left hemicolectomy the previous year) and a right-sided thoracoplasty for tuberculosis. She smoked 20 cigarettes a day. Laparotomy was performed for bowel obstruction, and multiple fistulae and perforations on the small and large bowel were discovered. Three small bowel resections were performed. Total parenteral nutrition (TPN) was instituted on the third day after operation, with 2500 ml of a solution that contained 2800 kcal and 16.5 g of nitrogen (Baxter Health Care Ltd.) to which was added ascorbic acid, 'solvito' and heparin. The $Paco_2$ had increased from 6.12 to 11.54 kPa, with a tachypnoea of 60 breaths per minute after 48 hours of this regimen. The patient's trachea was intubated and synchronous intermittent mandatory ventilation started with 40% O_2 with a minute volume of 5 litres. Spontaneous respiratory rate remained at 20–40 breaths/minute until the 12th day despite adequate oxygenation. Withdrawal at that time of TPN resulted in a dramatic decline in spontaneous respiratory rate, within one hour. It was decided, in view of this dramatic change in respiratory rate, to reinstitute TPN cautiously. Therefore, she was given 100 ml of Aminoplex 12 (Geistlich), and her spontaneous respiratory rate increased from 15/minute to 35/minute; the rate again decreased within 30 minutes of stopping the amino acid solution. She was given a further 100 ml of Aminoplex 12 one hour later and the spontaneous respiratory rate again increased from 15 to 35 breaths/minute, and fell within 30 minutes afterwards. The next day she was given 500 ml of 20% dextrose followed by 500 ml of Intralipid 20 with no increase in respiratory rate. Reinstitution of the full TPN regimen again resulted in an increase in respiratory rate.

A shift from fat to glucose metabolism occurs with an increase in respiratory quotient from 0.7 to 1.0 when glucose is used as the main calorie source in TPN. Lipogenesis occurs, with increased CO_2 production,[1] and this may result in respiratory failure, especially in those with marked calorie depletion. However, in this case the changes in respiratory frequency have clearly been associated with the amino acid solutions. Weissman *et al.* have shown increases in ventilation and metabolic rate 4 hours after starting amino acid infusion in subjects who received 5% dextrose only for 7 days,[2] and postulate that these changes are as a result of an increase in the magnitude of the ventilatory response to arterial CO_2, as well as a decrease in the response threshold to CO_2 stimulation. Animal studies have shown increases in minute volume of ventilation on injection of isotonic amino acids into the fourth ventricle. This is thought to be caused by competitive inhibition of the uptake of tryptophan (a precursor of serotonin) by branch chain amino acids. Serotonin has an inhibitory effect on the respiratory centre in the fourth ventricle.[3]

This case illustrates the need to consider amino acid solutions as a possible aetiological factor in the genesis of respiratory failure.

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Resistance measurement and connectors

Swivel connectors have been introduced recently by Portex Ltd. and by Intersurgical Ltd. They are almost right-angled, about 98.5° and 103° respectively. Their resistance might be expected to lie between that of a curved Magill connector (MIE Ltd.) and a right-angled Cobb's type tracheal tube connector (Portex Ltd.). Resistance, conventionally in units of pressure-drop per unit flow, was estimated by measuring pressure-drop at steady air flows of 10, 20 and 30 litres/minute with each connector attached to a tracheal tube of suitable size. There was low resistance at low flow rates. The pressure-drop increased at higher flows and this measurement was invariably greater with the right-angled fittings. It was found with the swivel connectors that their resistance was nearly equal to that of the Magill curved connectors. It exceeded the arbitrary but reasonable limit for adults suggested by Nunn[1] only at 20 or 30 litres/minute with tubes of 7.0 mm. Both swivel connectors were entirely satisfactory with all tubes of size 7.5 mm or larger.

This simple technique allows a useful comparison to be made between breathing attachments. It is possible that a larger pressure-drop can occur with the tracheal tube in isolation than with the same tube in place in the upper airway.[2] The assessment of work imposed on breathing might be more appropriate.[3] This method can, nevertheless, be applied anywhere that air flows of up to 30 litres/minute are available. Flow rates higher than 30 litres/minute introduce greater pressure differences but do not alter the findings.

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Skin preparation and spinal headache

The reported incidences of post puncture spinal headache (PPSH) in obstetrics, even after a 26-G needle, is still high (0.1–5%).[1] The hypothesis of CSF leakage through the hole made in the dura by the spinal needle, proposed by Bier in 1899, is well accepted, but the exact cause of PPSH is still unknown.[2]

We decided to carry out a study to determine the role of Betadine in the aetiology of PPSH, assuming that PPSH after 26-G spinal needle is but a particular case of benign chemical meningismus caused by an unintentional Betadine contamination of the central nervous system.

Two-hundred-and-eighty-six parturients, ASA class 1–2, scheduled for elective or urgent Caesarean section under 0.75% bupivacaine spinal anaesthesia were included. All patients received 0.2 mg glycopyrronium intramuscularly and 30 ml 0.3 M sodium citrate orally one hour before the operation. In all cases a 26-G spinal needle was used. Each patient was assigned to one of two groups: Group 1 (n = 149), with routine Betadine skin preparation applied three times, and Group 2 (n = 137) in whom the Betadine was wiped off vigorously from the puncture site with sterile sponges and 50 ml sterile water. Nine patients from Group 1 (6.05%) developed a typical spinal headache, which began 36–48 hours later and was mild, self-limited, and lasted 2–4 days in most cases. None of the patients from Group 2, with skin clean from Betadine, developed PPSH.

It seems that PPSH after a 26-G spinal needle is a complication of an iatrogenic origin, where a small amount of Betadine that consists essentially of Povidone [polyvinyl-porrolidone groups with molecular weight 10 000–700 000 and a small amount of arsenic, lead (0.001%), heavy metals (0.002%), aldehydes (0.5%), nitrogen (12%) and free slow-release iodine][3] enters CNS directly, probably on the tip of the spinal needle and bypasses the blood-brain barrier, which normally is almost totally impermeable to metals and high molecular weight substances.[4]

Thus, PPSH after 26-G spinal needle could be avoided easily through the use of our simple and harmless washing technique or by replacing Betadine with a less toxic antiseptic.

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Repeated general anaesthetics in the presence of a large undiagnosed left atrial myxoma

We report an unusual case of repeated general anaesthetics in a patient with undiagnosed massive left atrial myxoma.

An asymptomatic 65-year-old woman was referred for excision of left atrial myxoma after echocardiography had demonstrated a large tumour, which almost filled the left atrium and showed systolic prolapse into the left ventricle (Fig. 1). The mass, which measured 8 cm by 7 cm, was excised without incident under cardiopulmonary bypass and confirmed histologically to be a myxoma.

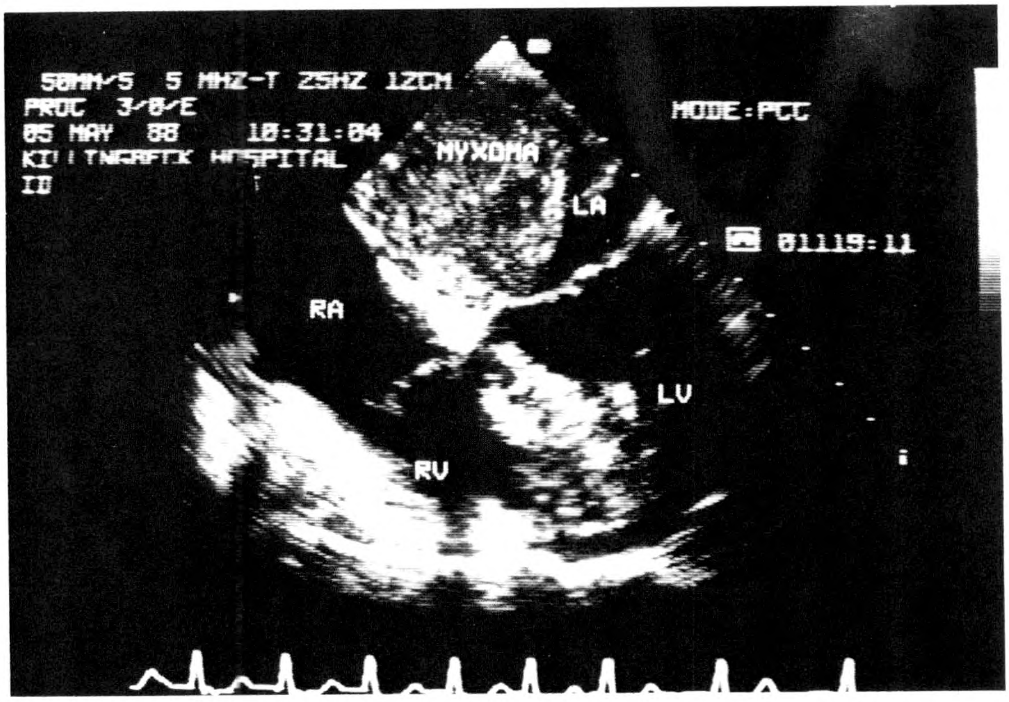

Fig. 1. Intra-operative transoesophageal cross-sectional echocardiogram showing myxoma filling the left atrium. RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle. Myxoma indicates position of left atrial myxoma.

It is of particular interest that she had undergone three general anaesthetics in the preceding 14 months, the first two for varicose vein surgery and the third for resection of ovarian carcinoma. A routine chest radiograph taken 5 weeks after gynaecological surgery showed a cardiac silhouette suggestive of mitral valve disease and she was referred subsequently for cross-sectional echocardiography which revealed the presence of a large left atrial myxoma. She denied all cardiovascular symptoms and no abnormal cardiac signs were documented before any of the previous general anaesthetics. The only anaesthetic complication occurred during resection of the ovarian carcinoma. Atrial fibrillation with a slow ventricular rate was noted after induction and persisted for the duration of the procedure reverting spontaneously to sinus rhythm.

It is clear from reports of the rate of myxoma growth that a significant tumour mass must have been present at the time of each of the previous general anaesthetics.[1,2] We suggest that use of the Trendelenburg position during each of the previous operations may have been responsible for the prevention of catastrophic occlusion of the mitral valve through the combination of increased venous return and gravitational effects on the atrial tumour.

Atrial myxomas are fortunately rare, but life-threatening tumours are now diagnosed with increasing frequency as cross-sectional echocardiography becomes more widely available.[3] Immediate excision is required to prevent embolisation or possibly fatal cardiac obstruction, and but for exceptional circumstances should take precedence over other operative procedures in the same patient. Our patient did survive three general anaesthetics despite an unsuspected atrial myxoma, but we believe it is prudent to undertake cross-sectional echocardiography in any patient with unexplained cardiac symptoms before general anaesthesia.

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Laryngospasm due to incomplete reversal not angina; a reply

The likelihood that residual neuromuscular blockade could cause laryngeal stridor, despite evidence of adequate reversal on clinical examination or neuromuscular stimulation, was reported earlier by Boliston.[1] Certainly incomplete reversal was a possibility in our patient, but Dr Margary (*Anaesthesia* 1988; **43:** 607) also acknowledges that residual curarisation alone is not enough to induce laryngospasm. Laryngeal irritation from intubation was thought in his cases to be an additional factor in causing spasm and anxiety. Sedation with diazepam or Entonox inhalation was effective in the relief of stridor.[2] Sedation and pain relief with papaveretum was only partially successful in our case, whereas subsequent sublingual glyceryl trinitrate spray abolished it completely. Therefore, as the principal cause of postoperative respiratory distress in our patient, severe acute angina remains an intriguing possibility.

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Assessment of epidural blockade

The article (*Anaesthesia* 1988; **43:** 557–9) surprised me. My concern is at the implied assumption that the midwives' assessment of the level of blockade was wrong if it did not agree with that made by the resident anaesthetist. In order to state that one party underestimated or overestimated the level of blockade requires assessment by an independent third party; this does not appear to have been the case. Virtually all of the assessments made by anaesthetic staff were carried out by junior anaesthetists; how well were their abilities at detecting the upper level of sensory blockade determined by the authors before the start of the study? The methodology is also open to question, since the assessment by the anaesthetist always followed that of the medical staff, and allowed the introduction of bias from patient familiarisation with the procedure. In addition, there were three times as many midwives involved as anaesthetists, militating against the midwives' becoming familiar with the technique of assessment.

The level of agreement between the two assessments as reported is encouraging, given the uncertainty inherent in the estimation of sensory levels which results from functional overlap of adjacent spinal segments. This study demonstrates that midwives are as capable as junior anaesthetists of assessing the upper level of epidural blockade; it is disparaging to suggest on the evidence presented that the midwives' assessments were in error.

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A reply

We thank you for the opportunity to reply to the letter from Dr Smith. The intention of our study was to show that with even a single period of instruction a midwife is as capable of assessing the upper sensory level after epidural blockade as a trainee anaesthetist and we feel that our results bear this out. All the midwives in our delivery suite were given the chance to learn this technique and we are pleased that so many of them accepted. This explains the difference in the numbers of doctors and midwives included in the study. There was no intention to determine which of the assessments was right or wrong and so the term 'estimate' was used and no third party was called upon to judge the issue. The midwives were asked to mark on the skin where the change in sensation to a cold stimulus was indicated by the mother. All the trainee anaesthetists involved had a minimum of one year's anaesthetic experience followed by at least one month's continuous experience in obstetric anaesthesia with intensive instruction on the assessment of epidural blockade using the technique described, and so were asked to estimate the dermatome levels of both measurements. It is possible that where differences occurred it was as a result of the speed at which the ice cube was moved across the skin, and the time taken to respond by the mother. We fully expect that accord would be reached as the midwives become more used to the technique. The fact that the level of agreement is so high after minimal instruction is, as Dr Smith says, encouraging.

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Allen's test and pulse oximetry

The report by Dr Rozenberg and his colleagues (*Anaesthesia* 1988; **43:** 515–6) on the Allen's test performed by pulse oximeter was interesting. They concluded that the detection of pulsatile flow by a Nellcor pulse oximeter confirmed a good collateral supply in the ulnar artery and therefore the radial artery could be cannulated with safety.

However, the study by Lawson *et al.* does not support this conclusion.[1] They measured flow using a laser Doppler flow probe in an arm occluded by tourniquet and found that a Nellcor pulse oximeter could detect a pulse at flows between 4% and 8.6% of baseline flows. Their data show that the pulse oximeter is a highly sensitive device for the detection of pulsatile flow but that no conclusions can be made as to the adequacy of that flow in terms of tissue perfusion and tissue oxygen delivery.

In cases of replanted digits it has been suggested that a slowly deteriorating haemoglobin saturation in the digit can be a useful way to detect subclinical ischaemia caused by venous outflow obstruction.[2] It is the change in saturation that is important and not the presence or absence of a pulse signal. Obviously the sudden loss of pulsations would coincide with the total loss of arterial flow.

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Complication of central venous catheterisation

The risk of disconnexion at the hub–shaft junction of any detachable catheter is well known.[1] Catheter embolism might follow. Disconnexion is a recognised complication of central venous catheterisation.[2] It is claimed that the detachable catheters are unable to withstand a pull of 25 Newtons at the hubshaft junctions when tested *in vitro*.[1] We experienced recently a disconnexion of Viggo 'Secalon' Universal central venous catheter which does not appear to have been reported with this particular brand of catheter.

A 32-year-old woman with hypertrophic obstructive cardiomyopathy had sudden ventricular fibrillation for which she was defibrillated. A Viggo 'Secalon' Universal catheter was inserted through the right internal jugular vein in order to monitor her central venous pressure. The tip position was checked on a chest X ray. The catheter site was found to be leaking the next day and on close examination it was found that the catheter had migrated completely inside the venous system after spontaneous disconnexion from the hub. A chest X ray demonstrated the proximal end of the catheter at a level of the right sternoclavicular joint and the distal tip was inside the right atrium.

The lost catheter in this case was successfully retrieved with the help of a Dotter basket[3] inserted through the right femoral vein.

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3. RAMSDALE DR, ARUMUGAM N, PIDGEON JW. Removal of fractured pacemaker electrode tip using Dotter basket. *Pace* 1985; **8**: 759–60.

A reply

The Viggo Secalon Universal catheter incorporates a separate attachable hub because it has been designed with long-term catheterisation and, more specifically, tunnelling in mind. It is essential, where a catheter is to be assembled to a discrete hub, that this be carried out according to the manufacturer's instructions and incomplete mating of the catheter and hub by the user, will render the connexion less than secure. The user can be confident that this union will remain intact if the assembly is completed according to the manufacturer's instructions and the union tested with a sharp tug.

The material used for the Secalon Universal catheter is polyurethane which is extremely strong; it has a breaking point in the region of 60 to 90 Newtons. When *correctly* assembled by the user, the connexion between the catheter and the hub will have a tensile strength between 30 and 50 Newtons. This is considered an improvement upon silicone elastomer predecessors of Secalon Universal, whose tensile strength was between 10 and 15 Newtons.

We are looking constantly at designs which will help avoid the connexion problems associated with this type of technique. Our current product does incorporate a feature that when the nut is tightened over the catheter/hub nose cone, the catheter is drawn further up on to the cone, thereby improving the connexion further.

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Tests for co-axial systems

The potential for a large increase in dead space if the inner tube of a co-axial system becomes detached has been appreciated in respect to the Bain system for some considerable time.[1] Indeed a test which enables the anaesthetist to check the integrity of the inner tube was described in 1977[2] and has been used regularly by myself. This is a report of a similar problem that occurred with a Blease Medical Open Co-axial system when used in conjunction with a Blease Brompton ventilator.

A Blease Major anaesthetic machine with the above ventilator and system was fully tested before the start of a major maxillofacial case. The 60-kg patient received controlled ventilation of the lungs with a fresh gas flow of 7 litres/minute and an $F\mathrm{IO}_2$ 0.4. A Blease Ventilator alarm was used with the disconnexion alarm set at 1.5 kPa and the overpressure alarm at 3.0 kPa. The patient, who had a history of angina, developed marked ST segment depression during surgery. This coincided with a decrease in his blood pressure from a systolic of 110 to 90 mmHg but no change in heart rate. He responded to an increase in his $F\mathrm{IO}_2$ and fluid to bring his pressure back up to 110 mmHg. The patient again developed ST depression within 20 minutes but now with T-wave inversion. The patient was noted to be cyanosed but continued with a stable heart rate of 80 and a systolic blood pressure of 90 mmHg. Oxygen (100%) was given and maintenance agents (propofol and alfentanil) were discontinued. Fentanyl 500 μg was administered slowly and the ST segment and T waves returned to normal. The surgery was by now well advanced but the surgeons were advised to perform the minimum necessary to enable us to discontinue the anaesthetic. Blood gases were performed because of the presence of cyanosis and revealed a pH 6.72, $P\mathrm{aCO}_2$ 31.0 kPa and a $P\mathrm{aO}_2$ 8.9 kPa $F\mathrm{IO}_2$ 1.0. The patient, tracheal tube, anaesthetic machine and ventilator system were then examined closely. The inner tube of the co-axial system was found to be detached at its proximal (ventilator) end. The patient was disconnected from this system and, after a stormy period during the correction of his respiratory acidosis, presented no further problems.

Co-axial systems such as the Bain continue to be popular in head and neck surgery. The development of the arrangement described above allows the anaesthetist to use a co-axial system with ventilators such as minute volume dividers. Checking the function of the ventilator with the system and the presence of a disconnexion alarm does not reveal a break in the integrity of the inner tube. My check now uses a slight modification of the technique described for the Bain system.[2] The inner tube has a 22-mm male taper fitting; this is connected to the common gas outlet of the anaesthetic machine using a 22-mm female:female adapter such as that found packaged with the Wright's Respirometer. A flow of 6 litres/minute of oxygen is then passed through the inner tube of the system and the distal (patient) end is occluded using the plunger of a 5-ml syringe. The oxygen Rotameter should be seen to dip and the machine pressure relief valve heard blowing off.

Several lessons can be learned from this incident. Unexplained cyanosis must be investigated; an oximeter might have alerted me earler. Secondly, this fault would have been detected immediately if a capnograph were available; perhaps use of this breathing system is unwise in the absence of a capnograph. Thirdly, use of the test described can at least assure the anaesthetist that the inner tube is intact at the beginning of each list.

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Intubation risk with patients with tracheostomy

Patients who have had a tracheostomy carried out often present for follow up procedures. The following case history describes a problem that arose when such a patient had her normal tracheostomy tube changed for the purposes of such a procedure.

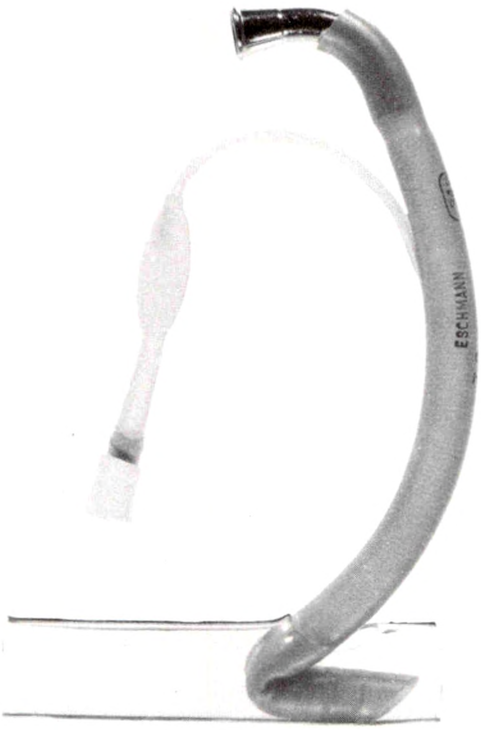

Fig. 1.

The patient was a 0-year-old woman with a laryngeal neoplasm who had an emergency tracheostomy carried out some months previously, for severe stridor. She had subsequently undergone radiotherapy and was now scheduled for microlaryngoscopy. Her general health was good and there was no history of asthma. Premedication was with morphine and atropine, and anaesthesia was then induced with thiopentone 250 mg and neuromuscular blockade achieved with vecuronium 6 mg. Her existing, noncuffed tracheostomy tube was then removed and a size 7, cuffed, latex-armoured tracheal tube was then passed through the tracheostomy. The change of tubes was felt necessary because of possible bleeding from above after laryngeal biopsy and so as to allow unimpeded inspection of the tracheostomy site.

There was no difficulty in passing the armoured tube; however on trying to ventilate the patient's lungs it was apparent that some form of obstruction was present and only minimal air entry occurred. There was no bronchospasm on auscultation and a problem with the tube was suspected. The cuff, which had been inflated slightly was fully deflated, but to no effect. The tube was therefore withdrawn slightly, at which point a sudden 'give' was felt transmitted from the distal, unseen portion of the tube. There was then no difficulty in ventilation and the procedure continued uneventfully. The tube showed no defect on later examination, but it was possible to bend the tip back on itself (Fig. 1). It seems probable therefore, that this had occurred in this patient, when the tube had reached the posterior wall of the trachea and had been at such an acute angle that the tip had kinked over.

This problem is almost impossible if a long suction catheter is used as a guide over which tracheal tubes are inserted or withdrawn in such patients.

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C.C. CALLANDER

Epidural blood patch for the pyrexial patient

May I offer an opinion in response to the enquiry by Dr Barker and colleagues? A counsel of caution should prevail, if only on medicolegal grounds. We have, fortunately, been placed in your correspondents' predicament only twice, and have then declined to offer a patch. We have provided a patch for the treatment of a postural headache (after either a spinal or an inadvertent dural puncture) for 348 patients. Invariably an extra quotient of blood is sampled through the same intravenous needle and submitted for culture. There has been only one positive culture, of the commensual *staphylococcus albus*, and no harm resulted. The investigation is undertaken as a forewarning, should the patient be incubating an infection.

There is a paradox here. Blood is shed into the epidural space in approximately 0% of administered epidurals. It is well known, as Barker *et al.* suggest, that bacteraemia, with or without accompanying pyrexia, is a frequent concomitant of labour, delivery and the puerperium. We have reported one case[1] of an epidural abscess from which was cultured an organism identical to that cultured from a high vaginal swab taken 2 weeks previously (and 2 days post partum). The absence of other reports of such a sequence is surprising since the blood shed at insertion of the epidural must provide a potential nidus for circulating bacteria. Fortunately the hazard appears to be very remote, but I would not tempt the gods by actually injecting blood from a patient who gave, at that time, evidence of a generalised infection.

The Birmingham Maternity Hospital,
Birmingham B15 2TG
J.S. CRAWFORD

Reference

1. CRAWFORD JS. Pathology in the extradural space. *British Journal of Anaesthesia* 1975; **47:** 412–5.

Editor's note. This letter was received shortly before Dr Crawford's untimely death.

Defects in epidural catheters

I was summoned to our labour ward to insert an epidural for analgesia in a labouring primigravida while in the middle of reading the letter by Dr S. Anderson[1] about defects in epidural catheters. A 16-G Tuohy needle was inserted into the epidural space and the catheter threaded through the needle after the usual precautions were taken of assessing patency of the epidural catheter. An impassable resistance was felt at 2.5 cm from the distal end of the catheter which inhibited removal of the Tuohy needle. Closer examination revealed an expansion of the outer diameter of the catheter as Dr Anderson described in her case reports. This defect proved to be of only minor inconvenience since the distal portion of the catheter could be excised without unduly compromising the length, but would have necessitated resiting the epidural had the expansion occurred more proximally.

This case reinforces the need to perform the simple task of ensuring that the Tuohy needle is patent for the entire length of catheter and that no one make of epidural system is immune from fault. Our hospitals use the Portex minipack epidural system and this is the first such problem that I or my colleagues have encountered.

Bristol Royal Infirmary,
Bristol
S.J. VALENTINE

Reference

1. ANDERSON S. Defects in epidural catheters. *Anaesthesia* 1988; **43:** 604–5.

Safer fibreoptic intubation

In their article fibreoptic intubation, (*Anaesthesia* 1988; **43:** 410–3) Drs Coe *et al.* state that they give suxamethonium to their patients when the scope is in the trachea. This is intended presumably to facilitate the passage of the tracheal tube through the glottis. We suggest that this represents a flaw in their technique since the patient may be put at risk of hypoxaemia if there is a delay in intubation. For instance, the tracheal tube may be too big, or the scope may flick out of the larynx as the tube is railroaded down, or the passage of the tube may be obstructed by the bevel impinging on the arytenoids or on the anterior wall of the trachea. Surely, a great advantage of fibreoptic intubation is that spontaneous ventilation can be maintained until the tube is in the trachea?

Our experience is based upon the population of patients treated in Maida Vale Hospital for disease of the craniocervical junction and cervical spine.[1] These patients are often Grade III or IV at laryngoscopy.[2] Our most effective technique to date, is a combination of deep inhalational anaesthesia, and topical anaesthesia of the glottis and trachea with lignocaine injected through the scope. We do occasionally encounter difficulty in railroading the tube, either because it is too large, or because the laryngeal reflexes are obtunded inadequately. The situation may be rectified at leisure by substitution of a smaller tube or by deepening the level of anaesthesia in the presence of spontaneous ventilation.

May we mention two further practical points which we have found helpful. Firstly, the application of xylometazoline (Otrivine) nasal spray which may be given with the premedication. This decongestant is effective and, unlike cocaine, relatively nontoxic. Secondly, the routine use of a lens demister/cleaner available from any optician or chemist.

Maida Vale Hospital,
London W9 1TL
H. HILL
I. CALDER

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The recent article (*Anaesthesia* 1988; **43:** 413–5) was a welcome item on what can be a difficult procedure. The problem encountered in the 18-year-old girl with Still's disease (Juvenile Chronic Arthritis—JCA) was the classic sequence of events as described in correspondence from our centre where JCA patients appear weekly.

The maintenance of tongue muscle tonus and a patent airway in these patients is commonly not possible with thiopentone and inhalational agent technique. Awake intubation is inappropriate in the younger JCA patients and the sedation required to allow them to tolerate it is enough in itself to obtund the airway. We have found ketamine the ideal agent to both preserve the airway[1] and permit fibreoptic nasal intubation.[2] I personally would not use suxamethonium in JCA patients during fibreoptic nasal intubation since, if for some reason it proved impossible to railroad the tracheal tube into the trachea despite first having visualised the larynx, it might be impossible to ventilate by mask should the need arise. Better to preserve spontaneous breathing and spray lignocaine on the trachea and vocal cords through the side arm of the fibrescope. After a short pause, the vocal cords will not react unduly to the passage of the fibrescope.

The technique is primarily for use with patients whose tracheas are impossible to intubate directly and these same patients are those in whom suxamethonium is best avoided, so surely a training technique should also avoid the

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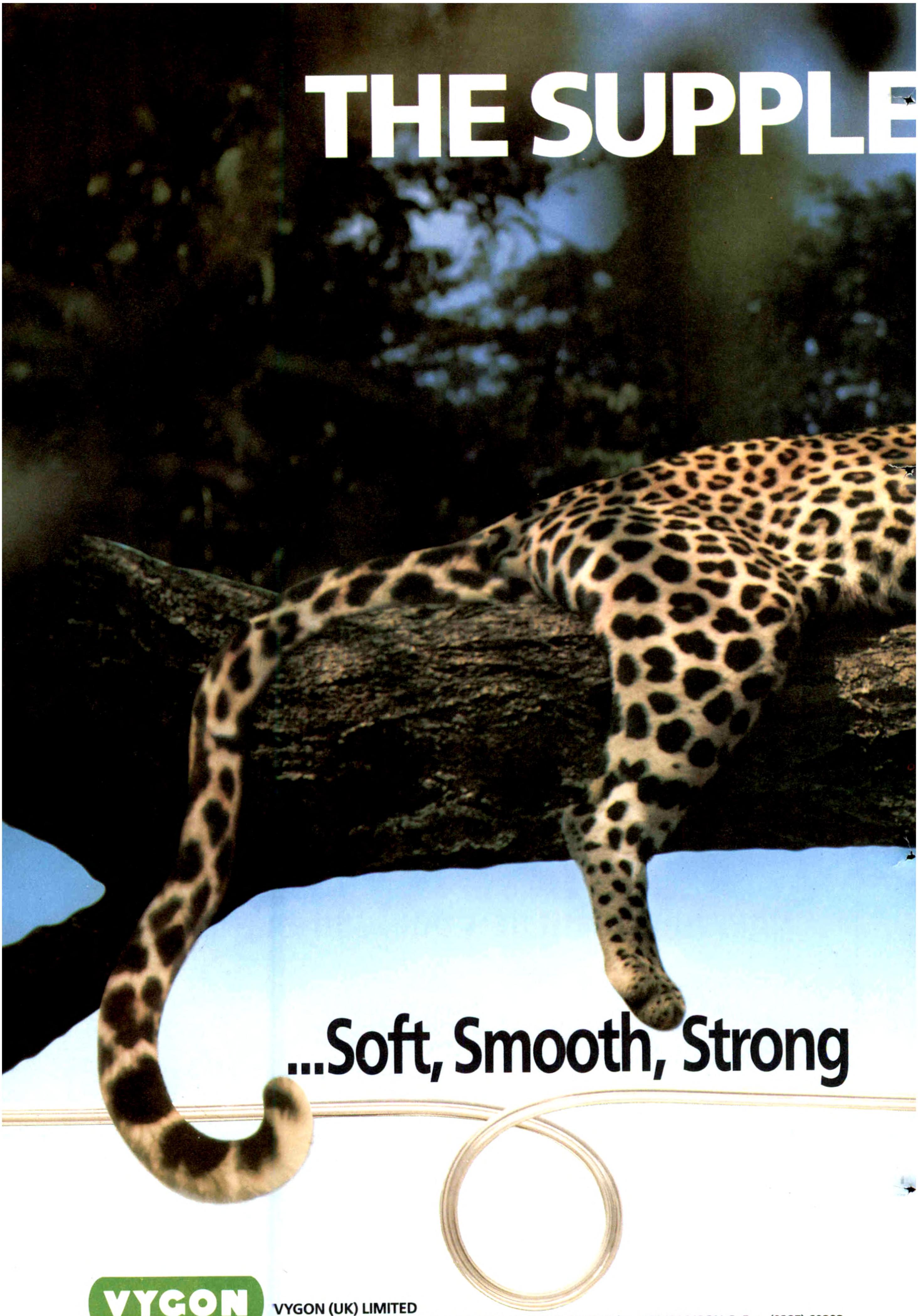

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easy option of suxamethonium during practice on normal patients?

Wexham Park Hospital,
Slough,
Berkshire SL2 4HL

B.L. SMITH

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The advantages of being competent with a fibreoptic instrument are by now accepted by all, but the reality is somewhat different. Skill and expertise in fibreoptic intubation still lie in the hands of a few enthusiasts. Aside from the ubiquitous problem of cost, I believe that it is the difficulty of gaining experience that has prevented wider dissemination of fibreoptic skills. It has been suggested that a minimum of 30 intubations should be completed before any degree of competence can be assumed.[1]

The recent report by Coe, King and Towey (*Anaesthesia* 1988; **43:** 410–3) describes an ingenious technique that allows continued ventilation of the lungs while nasotracheal fibreoptic intubation is undertaken at leisure. This represents a useful advance for teaching in patients about to undergo nasal intubation.

The nasal route has long been advocated in cases of difficult intubation for good practical anatomical reasons, but it must be admitted that there may be disadvantages from trauma, bleeding and increased airway resistance.[2] Most patients who present as potentially difficult to intubate can open their mouths enough to admit a tracheal tube and do not need nasal intubation for surgical reasons. The majority of surgical patients are intubated orally. Received opinion is that fibreoptic intubation is best carried out by the nasal route,[3] but the oral route is advocated for difficult intubation.[4]

To ensure that fibreoptic intubating skills are more widely dispersed it would be an advantage if useful learning experience could be gained on the large numbers of patients scheduled for orotracheal intubation. I have undertaken fibreoptic orotracheal intubation in 120 consecutive elective general surgical patients who ranged in age from 15–85 years and in weight from 40–110 kg in order to test feasibility.

Premedication was with temazepam 10–20 mg orally 1–2 hours pre-operatively. Anaesthesia was then induced using thiopentone 3–5 mg/kg, vecuronium 0.1 mg/kg. After ventilation of the lungs by facemask with N_2O 66% in oxygen and enflurane for 2–3 minutes and optimal positioning in the 'sniffing the morning air' position an assistant picked up the tongue gently with Magill forceps and pulled it forwards holding it in a piece of gauze between finger and thumb. The tip of the instrument (an Olympus BF Type B2 bronchoscope) with a suitable tracheal tube mounted was inserted into the mouth and passed backwards over the tongue keeping strictly in the midline. Passing behind the epiglottis brought the laryngeal inlet and vocal cords into view and it was usually possible to advance into the larynx and trachea without delay. Thereafter, the tracheal tube was advanced into position by railroading.

The time taken from insertion of the instrument to completion of intubation was taken as a crude index of ease or difficulty encountered. Predictably, there was a fairly steep learning curve. There were seven occasions when the time exceeded one minute in the first 40 cases, maximum 6 minutes, whereas in the last 40 patients there were no occasions when the procedure took more than 60 seconds. Suboptimal conditions were associated with poor positioning (inexperienced assistant who needed to apply more mandibular traction), excessive salivation and (or) obesity when pharyngeal laxity limits the view.

The technique has been used on four occasions when difficulties were documented with previous intubations. Suxamethonium 1 mg/kg was used as relaxant in these patients after the ability to inflate the patient by facemask had been established. In each case the procedure was rapidly successful.

This experience suggests that fibreoptic intubation by the oral route is not a difficult skill to learn or teach and is of much value in meeting the challenge of difficult intubation where the nasal route is not otherwise indicated.

Queen Elizabeth Hospital,
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A.P. JACKSON

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A reply

We are glad to see the interest generated by our article. We consider, however, that there may be some misunderstanding about the role of this anaesthetic technique. We advocate this method to teach novices how to perform fibreoptic intubation on *normal subjects*. Therefore, if there were any difficulty advancing the tracheal tube over the fibrescope, after administering suxamethonium, the procedure could be abandoned and intubation performed in the routine manner. However, as we mentioned in the article, we have found it very easy to ventilate the patient's lungs by way of the chimney airway, after suxamethonium administration, until the cuff is inflated on the tracheal tube. Our current practice is to ventilate the patient via the airway with 100% oxygen, to cover the period of railroading. We consider that in a normal subject there should be no difficulty in performing ventilation at any point and thus, no risk of hypoxaemia.

In the fibreoptic intubation of patients known to be difficult to intubate conventionally, such as those described by Drs Hill and Calder, we would agree that abolition of spontaneous breathing is potentially hazardous, and accept that topical anaesthesia of the larynx enables safe railroading of the tracheal tube. We would not advocate the use of muscle relaxants in such patients.

However, in the situation of teaching novices to perform fibreoptic intubation on normal patients, we need not rely on the use of deep inhalational anaesthesia and topical local anaesthesia, and in this situation the use of suxamethonium is justified.

We have performed fibreoptic intubation by way of the oral route, and agree that it is useful in some situations, such as paediatric intubation. We have found the nasal route to be easier for novices to learn, and having gained experience with this route they can progress to the oral route.

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P.A. COE

Guy's Hospital,
London
R.M. TOWEY
T.A. KING

A modified double-lumen tube

Prevention of obstruction of the left upper lobe is of clinical importance when a left-sided double-lumen tube is used.

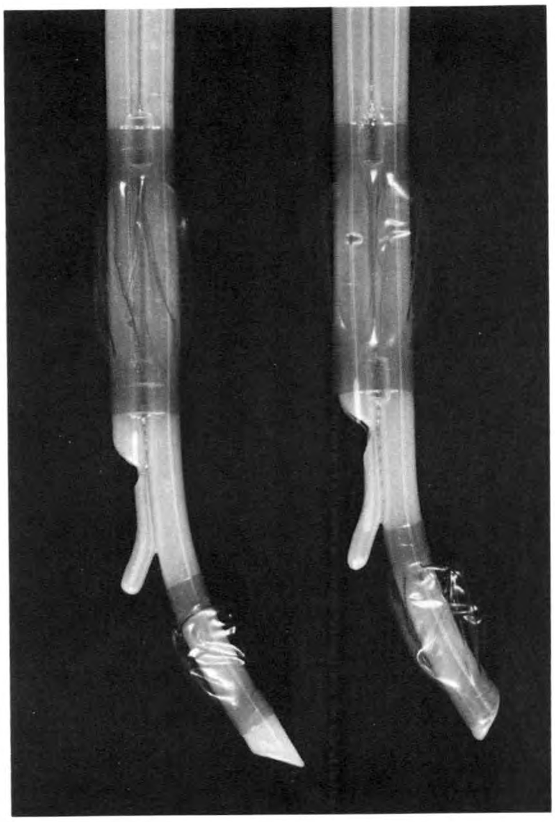

Fig. 1.

We have used plastic left-sided double-lumen tubes with carinal hooks (Twin Lumen Tube, Portex, Hythe, UK) (Fig. 1, left). The engagement of the hooks on the top of the tracheal carina may both prevent the tube from going too far into the left main bronchus during intubation and minimise the movement of the tube after placement, because flexion and extension of the neck can induce malposition of a previously well-positioned left-sided double-lumen.[1] However, when the hooks were seated on top of the tracheal carina, our fibrescopic examination has revealed occasionally that the tip of the left tube obstructed the orifice of left upper lobe, that is, the distance between the left tip and hook exceeded the length of left mainstem bronchus. We therefore cut the tip of the left lumen left-bevelled (Fig. 1, right) and reduced the length between the proximal left cuff and the tip of the left tube from 40 mm to 25 mm, and between the hook and the tip of the left lumen from 50 mm to 40 mm, compared to the commercially available one (size 5.5). The left mainstem bronchial length is reported to range between 29 mm and 68 mm.[2,3] Therefore, even in patients who have minimum length of left mainstem bronchus (29 mm), this modified tube allows 4 mm. We have not experienced left upper lobe obstruction in left one-lung ventilation since we adopted this modified tube.

Kyoto University Hospital,
Sakyo-ku,
Kyoto 606,
Japan
K. KOMATSU
T. ARAI
Y. HATANO

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Sudden cardiac arrest during percutaneous nephrolithotomy

We have read with great interest the letter of Economacos *et al.* (*Anaesthesia* 1988; **43:** 42?) about sudden cardiac arrest during percutaneous nephrolithotomy. In our opinion the facts supplied in the letter do not sufficiently substantiate the theory of disturbances of electrolyte balance as a result of absorption of the irrigating fluid. Furthermore, absorption of distilled water does not usually cause electrolytic disturbances in the plasma because it is dispersed among the body fluids.[1]

We offer an alternative hypothesis, based on the data given in the letter, for the cause of this fatal dysrhythmia. We believe that premedication with 0.1 mg fentanyl and N_2O as the only maintenance is insufficient to block the pain caused by surgery. Intense peritoneal irritation can cause bradycardia or other dysrhythmia as a result of reflex stimulation.[2]

The surgeon must be informed in such cases and must desist from painful stimulation. The anaesthetist must also seek other causes of bradycardia, (hypoxaemia or hypercarbia). Atropine should be used only if there is no improvement in the bradycardia, in adequate doses which would not exacerbate the condition.

Continuous epidural anaesthesia technique is used successfully during percutaneous nephrolithotomy in our department. It enables us to maintain communication with the patient, and effectively blocks pain for a considerable period after the operation.

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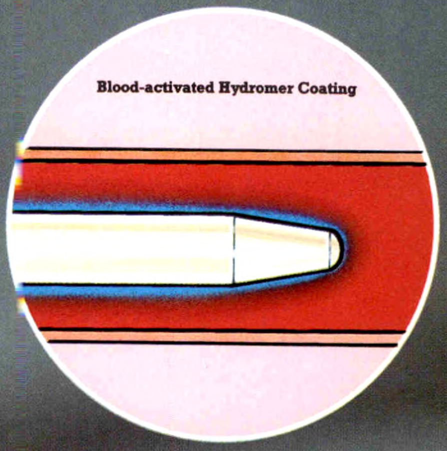

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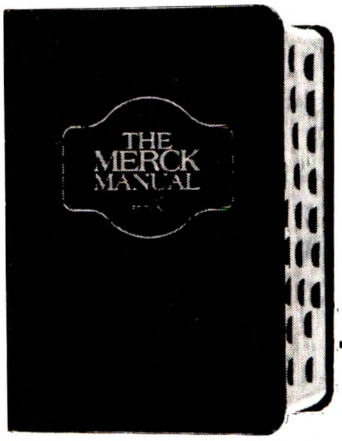

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Recently, two children whose lungs were ventilated after head injury and who were being weaned from controlled ventilation with Synchronised Intermittent Mandatory Ventilation (SIMV) with pressure support, were noted to be triggering a Servo 900C ventilator repeatedly.

A 7-year-old was reported to be hyperventilating to an arterial $P\text{aCO}_2$ of 2.9 kPa, and a 6-year-old was triggering SIMV sufficiently regularly to produce an arterial $P\text{aCO}_2$ of 3.1 kPa and yet would not breathe spontaneously if taken off the ventilator. The system was a Servo 900C ventilator, Fischer Paykel MR 600 humidifier and EME infant breathing system. Examination revealed the cause to be a small amount of water in a dependent loop of the expiratory limb.

The water occluded the expiratory limb at its lowest point and was lifted upwards towards the expiratory valve during expiration; at the end of expiration its swing back down was sufficient to reduce the pressure measured by the expiratory transducer below the setting of the trigger sensitivity control (below PEEP) necessary to prevent autotriggering. It was therefore decided to investigate the hypothesis that water in the expiratory limb of the breathing system could oscillate and that the resulting pressure changes be interpreted by the ventilator as spontaneous respiratory effort and produce triggering of a pressure supported breath.

A BOC Medishield lung simulator (compliance 0.2 litre/kPa, resistance of 0.4 kPa/litre/sec) was ventilated with a Servo 900C using the system described above. The signals from both inspiratory and expiratory pressure transducers, available at the 37 pin D connector on the back of the ventilator, were recorded on a high-speed pen recorder. One ml increments of water were added to the expiratory limb of a previously dry system while the pressure traces (Fig. 1) and the trigger sensitivity (below the set PEEP) just necessary to prevent triggering were recorded (Table 1).

Table 1.

Volume of water added (ml)	Setting of the trigger sensitivity control (below PEEP) necessary to prevent triggering (kPa)
0	0
1	0
2	0
3	0.1
4	0.25
5	0.4
6	0.5

The Servo 900C ventilator, when used in its SIMV mode, provides a preset minute volume and, as far as possible, synchronises its inspiratory phase with the patient's respiratory effort. The patient is also able to breathe spontaneously between the mandatory breaths and the ventilator provides fresh gas at the set PEEP pressure.

If 'SIMV-with-pressure-support' is selected, the fresh gas flow, when triggered, is supplied at the pressure support setting above PEEP. The ventilator independently monitors flow and pressure in both inspiratory and expiratory limbs of the breathing system. In SIMV and pressure support modes the fresh gas supply is triggered when the pressure measured by the *expiratory* pressure transducer decreases below the trigger sensitivity setting (which is itself below the PEEP setting, if PEEP is in use). Gas is supplied at the support pressure (above PEEP) until flow decreases below 25% of its initial value when flow is triggered.

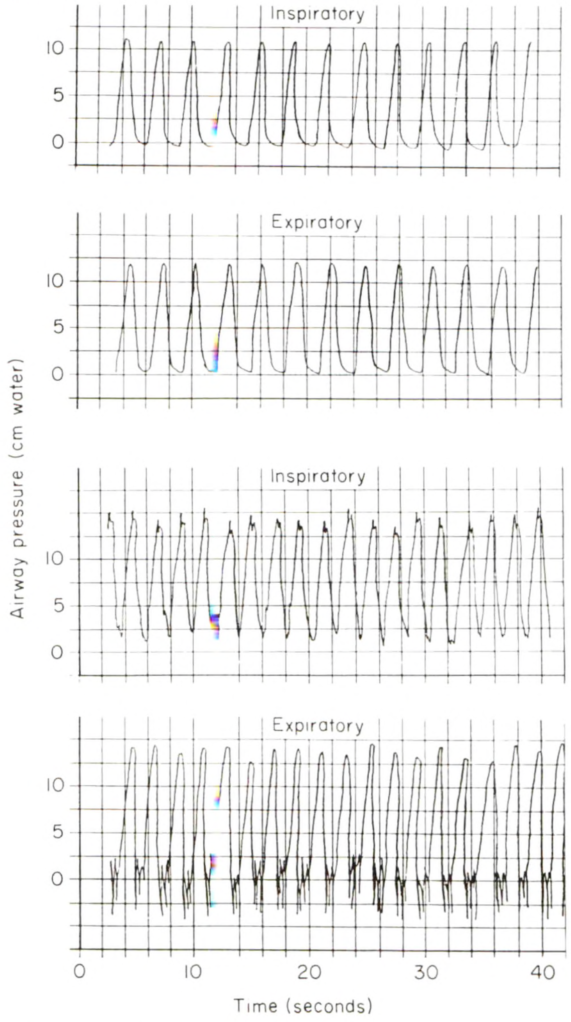

Fig. 1. Simultaneous inspiratory and expiratory pressure traces from a Servo 900C, ventilating a BOC Medishield lung simulator (rate 20 per minute, tidal volume 200 ml). The upper pair of traces were obtained with a dry system, the lower two after the addition of 3 ml of water to the expiratory limb. Note oscillations in the airway pressure in the bottom recording and note the increase in respiratory rate.

If there is sufficient water in a loop in the expiratory limb to occlude the lumen, then it will be lifted during expiration towards the ventilator. This column will swing down at the end of expiration and close the expiratory flap valve and reduce the pressure in the *expiratory* limb below the trigger threshold, (the pressure in the inspiratory limb would rise!). A pressure-supported 'spontaneous' breath is thus supplied. As soon as a triggered, supported breath is complete, the expiratory valve opens and the cycle repeats itself without an expiratory pause. There is thus an increase in respiratory rate, which is now dependent on the patient/breathing system time constant. As a result even a lung simulator may be interpreted by the Servo 900C as making spontaneous inspiratory efforts (Fig. 1).

To produce a drop in pressure at the expiratory transducer, any water in the expiratory limb must be moved during expiration and therefore there must be sufficient to occlude completely the lumen. The diameter of the infant system is 11 mm compared with 22 mm for the adult and thus occlusion of the former is produced by a much smaller volume of water.

An increase in the pressure measured by the inspiratory transducer is not seen since the compliance of the system on the inspiratory side of the water (system/lung/humidifier) is much greater than that on the expiratory side. This potential problem may be avoided by the inclusion of water traps in the breathing system, ensuring that they are positioned at the bottom of any dependent loops. Alternatively, since the decrease in pressure as a result of water in the expiratory limb is not seen at the inspiratory pressure transducer, this problem would be avoided if the Servo 900C only interpreted a concurrent drop in airway pressure at both transducers as indicative of a spontaneous inspiratory effort.

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Another misconnexion

A patient was anaesthetised for a routine abdominal operation; the trachea was intubated and the patient connected to a Siemens Servo 900 ventilator for controlled ventilation of the lungs. Inspiratory movement of the patient's chest was seen, but no expiratory movement, and the expired minute volume meter continued to read zero. The patient was disconnected immediately from the ventilator and manually ventilated with a Bain attachment.

On inspection, the expiratory limb of the patient system, was found to have been attached inadvertently to the expiration outlet of the ventilator, to which was also attached a PEEP valve. The scavenging was attached where the expiratory limb of the patient system should have been. The one-way nature of the PEEP valve meant that this resulted in complete expiratory obstruction of the circuit.

No alarm was activated because the expired minute volume alarm setting is not usually set above zero until after the patient is connected to the ventilator. The high pressure alarm would eventually have been activated, but not without the danger of barotrauma. Interestingly, had the PEEP valve not been attached, the expired minute volume alarm would have been activated immediately because there would have been reverse flow through the pneumotachograph and a negative expired minute volume reading. The ventilator had been checked as usual before use, (the delivery of gases by the ventilator was ensured, and the high pressure alarm and the expired minute volume alarm were checked), but this does not detect expiratory obstruction.

A reservoir bag should be attached to the patient end of the system with the ventilator working, to exclude both inspiratory and expiratory obstructions when this ventilator is to be used.

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Allen's test

Recent correspondence (*Anaesthesia* 1988; **43:** 516) indicates that the Allen's test is a useful pre-anaesthetic test for patients who require cannulation of the radial artery. Experience in two cases in the past week has suggested to me that this is not so. The first patient was a fit, 50-year-old woman who required surgery in which hypotensive anaesthesia was indicated. There was no evidence of arterial vascular disease and Allen's test in both arms showed adequate collateral circulation. On insertion of a 20-g cannula into the left radial artery there was immediate blanching of the thumb and index finger which persisted until the cannula was removed.

The second patient was a 70-year-old man who was scheduled for repair of abdominal aortic aneurysm. Allen's test in both hands showed persistent blanching of the thumbs and thenar eminences on release of the ulnar artery: collateral circulation was inadequate by this test. An arterial cannula was therefore put in the brachial artery of the left arm and this was removed immediately after surgery. In the early postoperative period he had problems with severe hypertension and a glyceryl trinitrate infusion was set up. It was deemed necessary that direct arterial monitoring would be appropriate for this and therefore an arterial line was established. Unfortunately, there was lack of communication between theatre and ICU and the medical staff on ICU did not know of the previous Allen's test and inserted a left radial line. There were no adverse consequences to this and the whole hand remained well perfused during the period that the cannula was in place which was 24 hours.

I think these cases show that an Allen's test does not show whether it is safe or not to insert a radial cannula.

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Epidural syringes

The article by Leiman *et al.* (*Anaesthesia* 1988; **43:** 397–8) was interesting.

Failure to identify the loss of resistance had become minimal as a result of significant improvement in the quality of glass syringes in recent years. It was my belief and that of many other anesthesiologists that wet or dry, polished syringes provided the best operant conditions, especially wet ones, but this is now demonstrated to be a misconception. However, the authors have not evaluated another type of syringe known as Pulsator Epidural syringe which has become popular over the last 2–3 years. This syringe, manufactured by Concord Laboratories, Inc., possesses minimal friction between the walls, does not require polishing or wetting; does not permit polishing and in my experience has proved to be very reliable. It is also interesting to note that I have never encountered jamming of the plunger with the Pulsator syringes, which I have seen quite often with glass syringes. Even though the performance and efficiency of Pulsator syringes has yet to be compared rigorously with glass syringes it appears to be superior.

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Music while they work

This is thoroughly to endorse the approach of Dr Allen (*Anaesthesia* 1988; **43:** 426) in his offer of radio headphones to patients who undergo surgery using local or regional anaesthetic techniques.

The apparatus is so compact and cheap (often gratis with some commercial offers) that I have found it easier to keep a personal set to ensure its constant availability in whatever theatre I am working. It is always worth while to check the reception beforehand and choose the waveband least affected by the diathermy apparatus, if used. A poorly-tuned radio is very irritating.

More patients who accept regional anaesthesia than perhaps we care to question, are happy to be in full possession of their faculties so I omit premedication. The liberal use of oral or intravenous sedatives perhaps reflects more the anaesthetist's lack of communicative skills than the patient's requirements? It is a paradox that there is so much current literature which cites the benefits of wakefulness and minimal recovery requirements after regional anaesthesia while others compare and contrast recovery profiles, amnesic properties of various benzodiazepine/opiate adjuvants. We seem to accept without question the patient's desire to be wide awake only in obstetric practice.

One note of caution: from experience using epidural bupivacaine with lower limb surgery, an incomplete motor block may irritate the surgeon if the patient taps out the beat to some favourite music! In practice the use of radio headphones is an extremely enjoyable and satisfactory diversion for many patients and I recommend it.

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No static at all?

Dr Allen (*Anaesthesia* 1987; **43:** 426) invites comment with regard to the use of personal stereo radio headphones as an alternative to sedation during regional anaesthesia.

I tried a similar technique as a supplement to spinal, sciatic and femoral blocks for hip and knee replacement procedures but found the static produced over the radio resulting from the use of surgical diathermy unacceptable to the patients. Cassette playing however was not influenced by diathermy. Does Dr Allen anaesthetise for non-diathermy-wielding surgeons, or has he found a way of screening the personal radio apparatus from diathermy interference?

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The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

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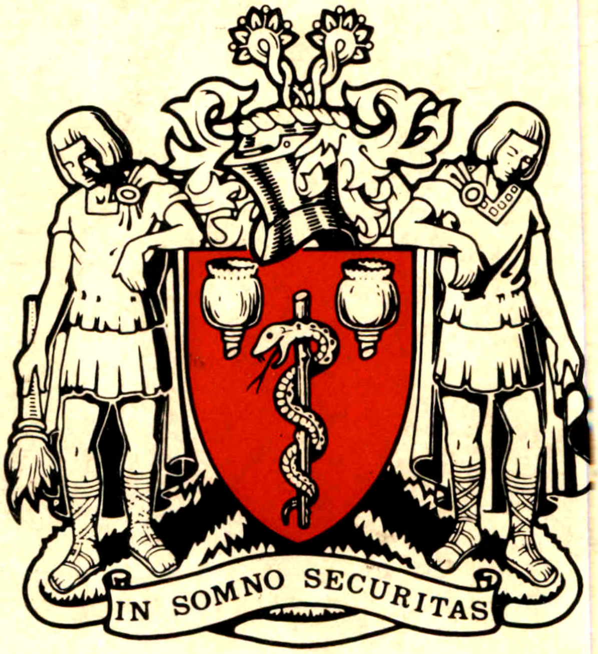

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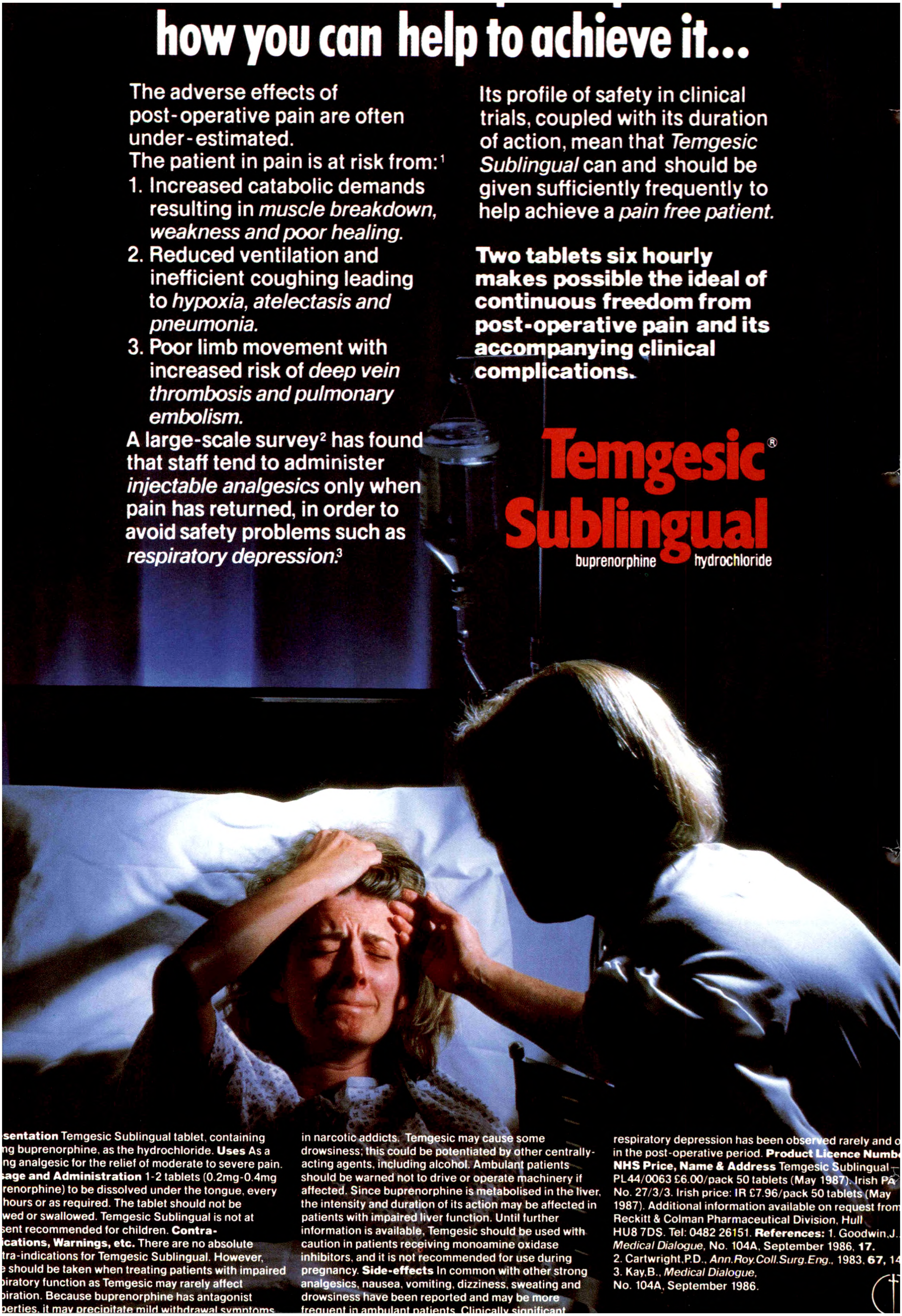

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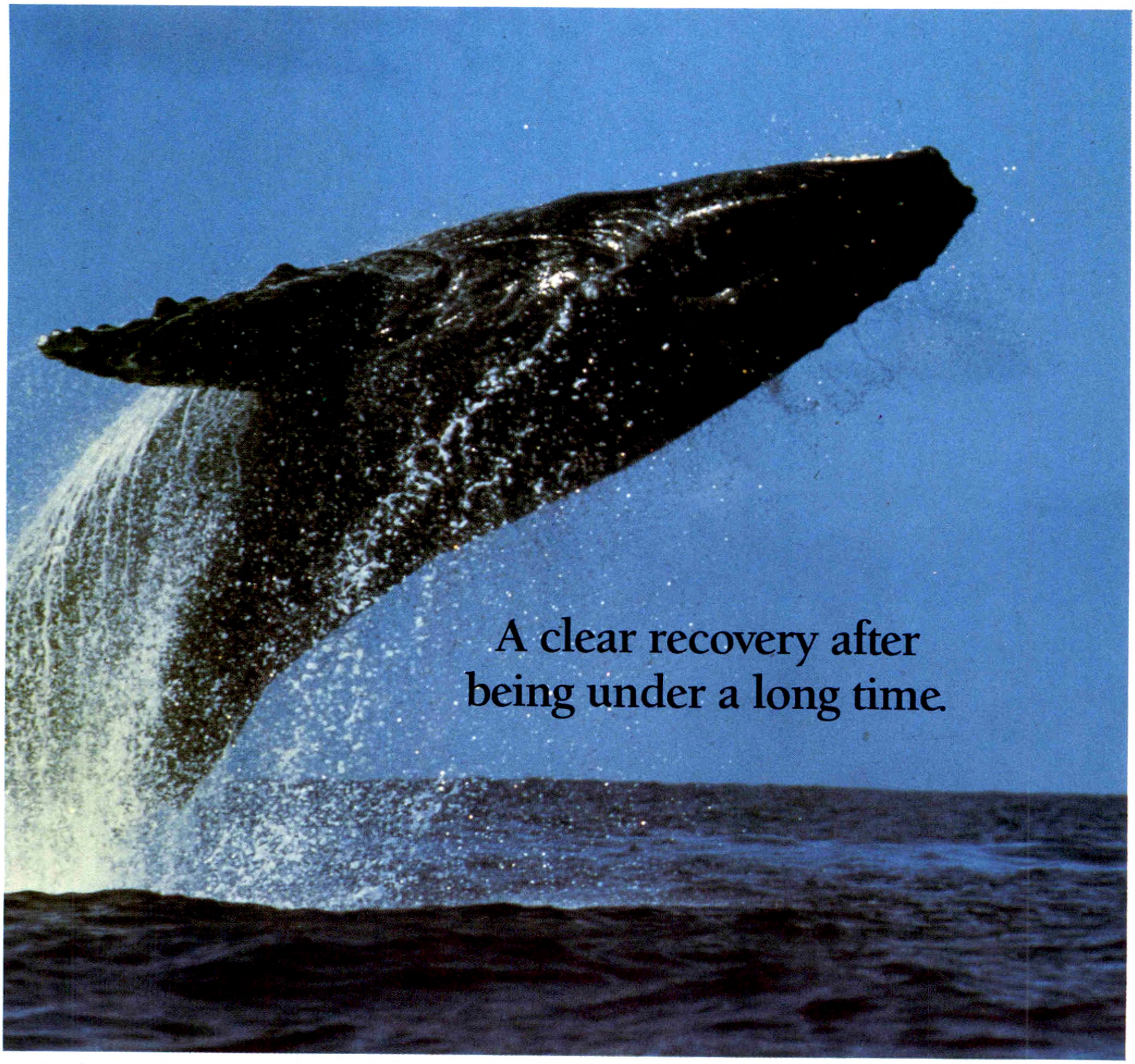

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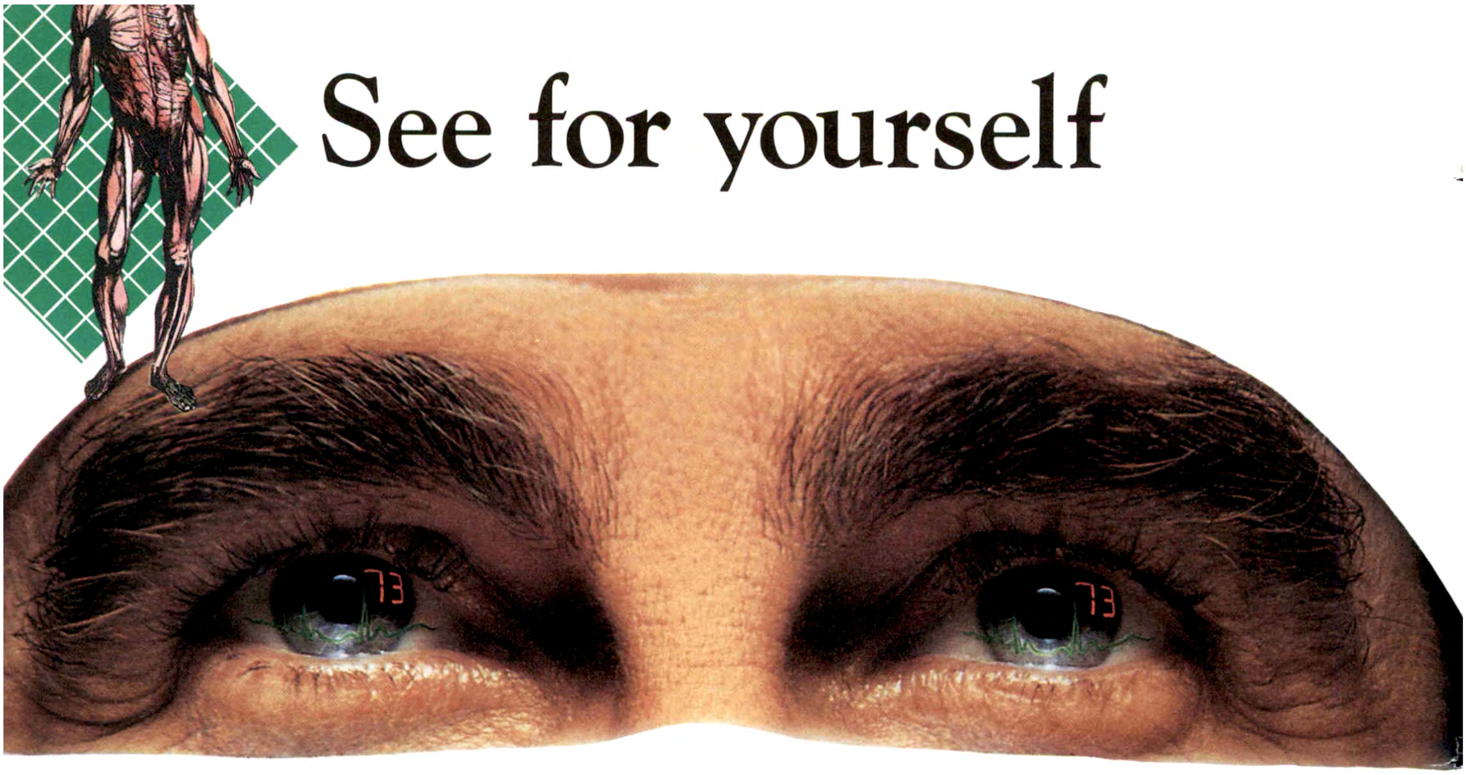

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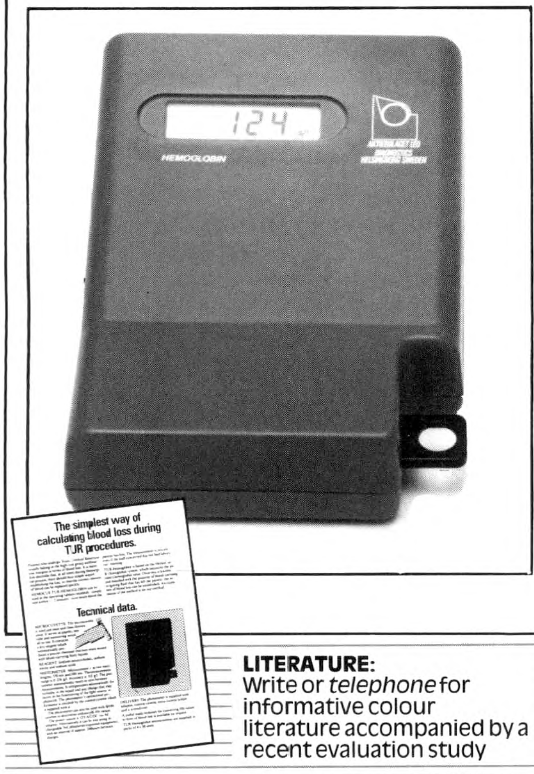
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Editorial

The College of Anaesthetists

The granting of 'Collegiate Status' to the Faculty of Anaesthetists by the Royal College of Surgeons a few months ago is an event of some importance, not only for anaesthetists and for medicine in general, but also for the public as well. It marks one further milestone on the road to maturity of a branch of medicine which, since its inception in 1846, has been perceived in varying degree, as a lowly and somewhat despised activity.

That the specialty had humble beginnings from the hospital porter and then the general practitioner has long ceased to cast a shadow. After all, the surgeon started as a barber and blood-letter, and the obstetrician as a man-midwife not very distantly related to the village handy woman. As for the physician, his antecedents may seem to be a little more respectable, but a host of shady characters, including the witch doctor and his modern descendants, might claim some blood relationship.

Change has very much been in the air. It is now as respectable to affirm the value of the anaesthetist as it is to affirm abhorrence to apartheid. If there are still remnants of a disparaging attitude, mostly among older surgeons, towards their anaesthetic colleagues, it will surely disappear in time. Fortunately, the anaesthetist's skills and knowledge, both clinical and theoretical, which make modern surgery possible, are now appreciated even by the public. It would require a foolhardy doctor without special training to undertake the administration of an anaesthetic, except in emergency, without first thinking of the social and medicolegal consequences of accident or worse.

The Faculty of Anaesthetists came into being in 1948 as an offshoot of the Royal College of Surgeons. It marked a big step forward, because it put the seal on the formal recognition already achieved in the National Health Service (NHS), and reaffirmed the interdependence of surgeon and anaesthetist. Anaesthetists will always regard the long period of association with the Royal College of Surgeons with gratitude. Those 40 years have brought acknowledgment, recognition, and respectability to the specialty. Training at the highest level has become organised, and examinations modelled on those of the Royal College of Surgeons have made the qualification of FFARCS universally recognised as the mark of the highly trained expert, and the minimum requirement for the aspiring consultant. Not the least of the multitude of benefits which stemmed from this association was the use of the Royal College buildings themselves. These dignified premises, with their aura of tradition, offered unrivalled facilities for meetings, conferences, and administration. The location of the Faculty became the envy of anaesthetists in other parts of the world.

In spite of the patent advantages, the arrangement of the Faculty as part of the Royal College of Surgeons was not ideal. It carried the stigma in the eyes of colleagues at home and abroad, particularly in Europe and the United States of America, that in Britain anaesthesia was an extension of surgery, and that anaesthetists in academic matters as well as clinical were tied to the apron strings of surgeons. There was a good deal of substance in that perception. The President and Vice-Presidents of the Royal College of Surgeons attended every quarterly Faculty Board meeting. Indeed they are still *ex officio* members of the Council of the new College of Anaesthetists. The minutes of the Faculty, were 'approved' by the College Council, and the Faculty finances were tied closely to those of the College. There was little or no representation of the Faculty as of right, on national committees concerned with numerous matters involving hospital services in the NHS. Advice from the Faculty usually had to filter through some other body such as the Royal College of Surgeons or the British Medical Association.

Gradually the situation changed. Chairs of Anaesthetics in the more forward looking universities were established, often in the face of considerable local resistance. These were occupied by scholars of international repute. Their activities as teachers, researchers, and clinicians, have resulted in what was at first a trickle of erudite papers, journals, books, and other contributions, but which soon became a flood. There is no longer any doubt that anaesthesia as an academic subject stands comparison by any standard, with other specialist postgraduate subjects in Medical Colleges. In the clinical field too, a generation of consultant anaesthetists have demonstrated that they are indispensable in a modern hospital. Can anyone, not least a surgeon, imagine a District General Hospital of today without its cadre of anaesthetists of all grades? Intellectually and technically they have proved themselves the equal of (and sometimes superior to) their colleagues in other branches of medicine.

At the centre of affairs, change has been continuous. In the Royal College of Surgeons, the Faculty gradually became more and more independent of the supervision of the Council of the College. A more relaxed and tolerant attitude within the College developed. Successful examinees were admitted to their Fellowship of the Faculty by the Dean of the Faculty, instead of by the President of the Royal College of Surgeons. Direct representation of anaesthetists on the College Council, and on numerous other public and statutory bodies became the normality.

The time appeared to be ripe for the independence of anaesthetists from any other specialty. They formed the largest single group of specialists within the NHS, and their work had spread over many hospital activities outside the operating theatres. A College of Anaesthetists seemed to be a normal and desirable development of the specialty. Such a College would confer the same benefits on its members as were enjoyed by the members of the Colleges of Physicians, Surgeons, and Obstetricians, and by those of the emerging Colleges of Pathologists, Radiologists, and General Practitioners.

Unfortunately there was little support from the anaesthetic establishment. Opposition to the idea came, surprisingly, from such least expected quarters as the

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Board of the Faculty itself, and from such influential centres as Oxford, London, and Liverpool. Every possible objection was raised, and the matter moved at a snail's pace. Many were the committees set up. Many were the bulky reports produced. Yet at the same time more than one poll of anaesthetists showed that there was, at grass-root level, a strong sentiment for the formation of a College of Anaesthetists.

The final weapon, always potent, concerned funding. The spectre of high annual subscriptions and the possibly crippling burden of upkeep of large and sumptuous premises, was paraded. The effect was predictable. The matter of a college went into hibernation.

A few years ago, an energetic and farsighted President and Council of the Association of Anaesthetists brought the matter to life again, and a Royal College of Surgeons Council, probably by now weary of the whole business, proved unexpectedly compliant. A sympathetic President of the Royal College of Surgeons helped the matter along, and a formula was devised that appeared to satisfy, at least to some extent and for the time being, the aspirations of the anaesthetists. On 19 October 1988, 'Collegiate Status' was conferred on the Faculty of Anaesthetists. On that day, the Faculty of Anaesthetists ceased to exist; its place was taken by the College of Anaesthetists. The Board of the Faculty became its Council, and the Dean became the first President. The FFARCS became the FCAnaes.

It remains to be seen whether the new arrangement of a College of Anaesthetists *within* the Royal College of Surgeons is the final step or just one further stage, and whether Collegiate Status means more than just a change of name. Let us hope that eventually the College will achieve the ultimate accolade of Royal patronage. Nevertheless, while not decrying the considerable significance of these events, it must be said for the record, that at the moment they do seem to fall a little short of that independence of which its innovators dreamed.

Most Fellows of the Faculty will have received a copy of extracts from the recently amended Charter of the Royal College of Surgeons, but may not have studied it in detail. It contains, *inter alia*, the following which clarify the present situation.

> '1(i) . . . that the composition of the Royal College of Surgeons as one corporate body having three constituent parts comprising respectively Surgeons, Anaesthetists and Dental Surgeons . . .'
>
> '1(ii) . . . that the enhanced status of the Anaesthetists within the Royal College of Surgeons and in the medical profession at large be recognised by designating the Faculty of Anaesthetists a College within the Royal College of Surgeons to be known as the College of Anaesthetists'
>
> '7(b) The Council may delegate to the College of Anaesthetists . . . such powers and privileges as may be conducive to the due promotion and advancement of the Art and Science of Anaesthesia . . . including powers to grant Diplomas of Fellowship in the College of Anaesthetists.'

The title, College of Anaesthetists, will be welcomed by all who have the welfare of patients, surgeons, and not least, anaesthetists themselves, at heart. Even if the present arrangements appear to be not quite ideal, they do represent a considerable advance in the development of anaesthesia. The new title adds dignity to the specialty and the feeling, if not the actuality, of independence. We must be grateful for what has been done by our leaders, and give them wholehearted support. The College of Anaesthetists remains housed in, and a part of, the Royal College of Surgeons, with all the advantages which that confers and with which we are familiar. However, the time will surely come when, like its sister Colleges, the College of Anaesthetists will also have its own home.

The future is bright, academically and clinically. Anaesthesia will continue to forge ahead, to the advantage of everybody in the community. Medical students will see even more clearly that anaesthesia is a worthwhile and respected career with every opportunity for the development of scientific or clinical aptitudes. Anaesthetists will more than ever play their part in the hospital community as specialists in a wide range of skills both in and out of the operating room. In time, the tensions which for so long have bedevilled relations between anaesthetists and surgeons will disappear, to the ultimate benefit of the patient.

The College of Anaesthetists deserves the continued support and blessing of everyone in hospital life. May it prosper and enhance medicine in general, and particularly, the already high standing of British anaesthesia.

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Editorial notices

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as an when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

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Neostigmine after spontaneous recovery from neuromuscular blockade

Effect on depth of blockade monitored with train-of-four and tetanic stimuli

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Summary

The effect of neostigmine on neuromuscular function was examined after spontaneous recovery from an atracurium-induced neuromuscular blockade, which reached a train-of-four ratio of either 0.5 or 0.9. Two doses of neostigmine 2.5 mg were given 5 minutes apart. Neuromuscular recovery was assessed with train-of-four and tetanic stimuli. The first dose of neostigmine antagonised the neuromuscular blockade. The second dose diminished tetanic height and increased tetanic fade. The train-of-four measured mechanically was adversely affected to a small degree, but when measured with the electromyograph no significant change occurred. Neostigmine may adversely affect neuromuscular function after spontaneous recovery from a non-depolarising block. This is unlikely with a single modest dose and any effects are probably short-lived.

Key words

Antagonists; neuromuscular relaxants.
Neuromuscular relaxants; atracurium, measurement of response.

An anticholinesterase agent such as neostigmine is routinely used to antagonise a non-depolarising neuromuscular blockade. Spontaneous recovery from muscle relaxation with the newer medium-duration neuromuscular blocking agents, atracurium and vecuronium, occurs earlier and more rapidly compared with the older relaxants. This has led one author to comment that 'the administration of neostigmine to a patient who has almost fully recovered is a common enough situation in the absence of neuromuscular monitoring'.[1] It is suggested[1–3] in this circumstance that neostigmine, instead of antagonising the block may increase it, and that 'neostigmine in clinical doses could be a potential hazard in anaesthetic practice'.[2]

Anticholinesterase agents, such as neostigmine, possess neuromuscular blocking properties in the absence of previously administered muscle relaxants.[4] Neostigmine, in a small number of patients, has been shown to increase tetanic fade when a considerable degree of spontaneous recovery from a muscle relaxant has occurred.[2] However, it is difficult to comment on the likely effect of this in terms of adequacy of muscle power and respiratory function. The degree of fade during a train-of-four (TOF) stimulation has been correlated with indices of clinical recovery of muscle function,[5] and changes in the TOF may therefore give a better guide to the clinically relevant changes in muscle power.

We wished to determine if the administration of neostigmine after spontaneous recovery from a non-depolarising blockade would adversely affect neuromuscular function. Different methods of stimulation and monitoring of neuromuscular function will give different results.[6] We used both tetanic stimulation measured mechanomyographically, and TOF stimulation measured mechanomyographically (MMG) or electromyographically (EMG). The neostigmine was administered when the neuromuscular block had reached a predetermined level, and the duration and degree of change in neuromuscular block were recorded. Fixed doses of neostigmine were used since this is probably more common in clinical practice than the use of weight-related dosage.

Methods

Twenty-nine patients of physical status ASA 1 and 2, aged 18 to 68 years (mean 33.8, SD 16.2), who weighed 44 to 89 kg (mean 67.2, SD 11.4) were studied. They required anaesthesia for elective surgery (dental extractions, 14 patients; varicose veins excision, four patients; hernia repair, four patients; minor gynaecological procedures, three patients; biopsy of node, three patients; and rhinoplasty, one patient). None of the patients had neuromuscular diseases or were receiving any drug known to affect neuromuscular function. The study was approved by the hospital ethics committee and written informed consent was obtained from all patients.

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Neuromuscular monitoring was performed on both arms in all subjects, and was started after induction of anaesthesia before neuromuscular blocking agents were given. On one arm a Datex NMT-100 Relaxograph[7] was used for stimulation of the ulnar nerve at the wrist *via* disposable pregelled silver–silver chloride surface electrodes, and for recording the EMG of the *adductor pollicis* muscle. The placement of the electrodes was as described by Carter *et al.*[7] Supramaximal TOF pulses of 0.1 msec width and a frequency of 2 Hz were delivered every 20 seconds. On the other arm the ulnar nerve was stimulated every 20 seconds through percutaneous needle electrodes using a Grass S88 stimulator and a stimulus isolation unit (SIU5). In these patients the stimulus either consisted of TOF square wave pulses of 0.2 msec duration at a frequency of 2 Hz or a 50 Hz tetanus delivered for one second.[8] Evoked force adduction of the thumb was transduced and measured using a Gould–Statham UC-3 force transducer with a 2.3-kg load for the TOF stimulation, and a 9.1-kg load for the tetanic response.[8] The measurements from both arms were simultaneously recorded on a two-channel recorder (Gould Mk220). Both arms were wrapped in cotton wool and dressing towels to maintain forearm skin temperature, which was measured with a YSI telethermometer.

Premedication consisted of papaveretum (10 to 20 mg) and hyoscine (0.2 to 0.4 mg). Induction of anaesthesia was with fentanyl (50 to 100 μg) and thiopentone 4 to 7 mg/kg. Anaesthesia was maintained with 66% inspired N_2O in oxygen and 0.5% inspired isoflurane, with increments of thiopentone (50 mg) and fentanyl (50 μg) if indicated. Isoflurane was measured with a Datex Normac anaesthetic agent monitor, and end-tidal CO_2 maintained between 4.6 and 6.0 kPa measured by a Datex Normocap monitor. Atracurium was administered when a stable baseline recording of neuromuscular function was established. Muscle relaxation was allowed to recover spontaneously to a predetermined level, at which point neostigmine 2.5 mg with atropine 1.2 mg was administered. Five minutes later a second dose of neostigmine (2.5 mg) with atropine was given and anaesthesia was continued for a further 10 minutes and until the T4:T1 ratio (the ratio of the fourth twitch over the first twitch of a train-of-four twitches) was at least 0.7. All patients were assessed clinically for muscle weakness before they left the recovery area, and were seen the next day on the wards if not previously discharged from hospital. The study was performed in two parts.

Part 1

Eighteen patients received an initial dose of 0.25 mg/kg of atracurium. Further increments of 5 mg were given if clinically required. Antagonism of the neuromuscular block with neostigmine was attempted when the T4:T1 ratio was 0.5 when measured with the EMG. In all patients a TOF was monitored with the EMG on one arm. The other arm was monitored with a force transducer (mechanoymography). Eight patients received TOF stimulation, and the remainder a 50 Hz tetanus stimulation delivered for one second. No usable readings were obtained because of equipment failure in one subject given a tetanus, and in another the readings were incomplete. These results have been discarded. The findings in this group are therefore based upon 18 sets of results for TOF EMG readings, and eight results each for force transducer measurements of TOF and tetanic stimuli.

Part 2

A further 10 patients were then studied. The initial dose of atracurium was 0.2 mg/kg. A smaller dose of atracurium was used in this part so that spontaneous recovery would occur within an acceptable period. In this group neostigmine was given when the TOF ratio measured with the Relaxograph was at least 0.9. As before, the EMG response to a TOF stimuli was recorded in all patients on one arm. Five patients received a TOF stimulus recorded mechanomyographically on the other arm, and the other five patients a tetanic stimulus.

One patient was anaesthetised in an identical manner with the sole exception that all muscle relaxants were excluded. Neostigmine and atropine were given as for the other patients when anaesthesia was stable. Recordings were made of the TOF measured both with the Relaxograph and the mechanomyograph.

Measurements

Measurements were taken immediately before the first dose of neostigmine (Neo), 2 minutes (Neo + 2) and 5 minutes later (Neo + 5, immediately before the second dose of neostigmine), then 2 (Neo + 7), 5 (Neo + 10), and 10 minutes (Neo + 15) after the second dose. The height of the first twitch of the TOF (T1) and the T4:T1 ratio were taken from the paper trace to measure the response to the TOF stimulus. The response to tetanic stimulation was measured by the height of the peak tetanic response (Tt) and the degree of fade (Tp:Tt), where Tp is the height of the plateau to which the tetanic response faded. The height of T1 and Tt for each patient was calculated as a percentage of the height of the final reading (Neo + 15), so that the height of T1 or Tt at Neo + 15 was 100%. Figure 1 shows a typical trace of simultaneous recordings of EMG TOF and MMG tetanic stimulation.

Analysis of results was performed using SPSS-PC. Repeated measures analysis of variance (Manova) was used to compare both Tl or Tt, and T4:T1 or Tp:Tt over time and between groups of patients given the anticholinesterase at the TOF ratios of 0.5 or 0.9. The first dose of neostigmine had no observable detrimental effect on any of the measurements of neuromuscular function, so we performed this analysis over only the last four time periods, that is, from Neo + 5 onwards. One way analysis of variance (Oneway) was used to test for differences between the groups with respect to age or weight, and the Chi-squared test for differences in the sex distribution. Selected paired *t*-tests were performed between the values at Neo + 5 and Neo + 7 (before and after the second dose of neostigmine) on the results from MMG TOF and tetanic stimuli.

Results

There was no significant difference between the groups with respect to age, weight, or sex distribution.

The dose of atracurium (0.25 mg/kg) administered to the initial 18 patients resulted in 100% block in eight, with an average maximum block in the remaining 10 of a T1 of

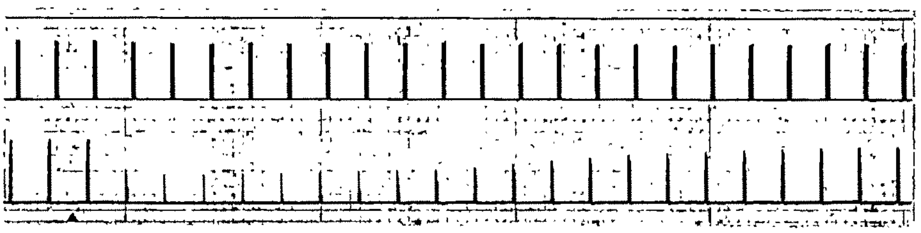

Fig. 1. Simultaneous recording of EMG TOF (upper trace) and MMG tetanus (lower trace). ▲, administration of second dose of neostigmine at which time the EMG TOF ratio had recovered to 1.0.

Table 1. Mean (SEM) results of neuromuscular function at administration of neostigmine measured simultaneously on left and right arm. All patients had TOF measured with the EMG, and either TOF with MMG or tetanic stimulation with MMG. Values expressed as mean (SEM).

Method of measurement	Number of patients			
	8	10	5	5
EMG TOF ratio	0.51 (0.008)	0.52 (0.006)	0.93 (0.007)	0.93 (0.004)
MMG TOF ratio	0.47 (0.03)	—	0.81 (0.08)	—
MMG Tet Tp:Tt ratio	—	0.60* (0.06)	—	0.96 (0.03)

Tet, tetanic stimulation; Tt, peak tetanic tension; Tp, plateau twitch height at end of tetanus.
*, $n = 8$.

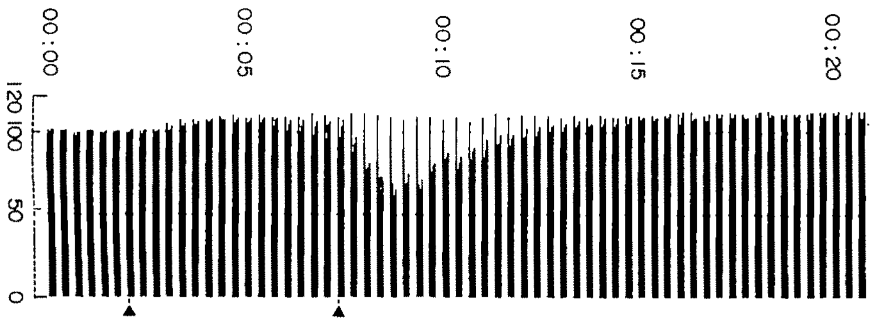

Fig. 2. Relaxograph trace of patient given two doses of neostigmine in the absence of any muscle relaxant. ▲, administration of neostigmine 2.5 mg + atropine 1.2 mg.

5.3% of control. Fourteen of these subjects received one dose of muscle relaxant before the neostigmine was administered, and in these patients the mean time to recover to a TOF ratio of 0.5 measured with the Relaxograph was 41.3 minutes. Ten patients were given atracurium 0.2 mg/kg. One achieved 100% block and the others averaged a maximum block of T1 of 5.3% of control. Six of the 10 patients given neostigmine at a TOF ratio of 0.9 measured with the EMG had only one dose of relaxant, and the mean time to reach this ratio was 48.4 minutes for these patients.

Both arms were monitored in every patient, so pairs of readings using the different methods of measurement were recorded. Table 1 shows the mean of readings from the same patients at the points at which the first dose of neostigmine was administered.

Neostigmine in the absence of neuromuscular blockade

One patient was studied in this way. Figure 2 shows the Relaxograph tracing for this patient. There was a greater increase in the height of T1 compared with the increase in the height of T4 after the first dose of neostigmine. This resulted in a slight decrease in the T4:T1 ratio. However, the second twitch of the TOF (T2) was consistently smaller than either T1 or T4. There was no alteration in the height of T1 after the second dose of neostigmine, but the T4:T1 ratio decreased markedly before recovering within 10 minutes. The same result was observed with both the EMG and the MMG. Monitoring was continued for a further one hour and 25 minutes during which time the TOF ratio remained at 1.0 and the T1 at 112% of baseline. Fasciculations similar to that observed after suxamethonium were noted in the face, arms and legs approximately 3 minutes after the second dose of neostigmine. They lasted approximately 10 minutes. The patient's cardiovascular system was stable during this period. No weakness or any other abnormalities were noted in the recovery room. The patient had no postoperative complaints and recovered normally. However, in view of the observed fasciculations, this part of the experiment was not repeated.

Measurements of EMG TOF (Figures 3 and 4)

When neostigmine was administered at a TOF ratio of 0.5, the first dose of neostigmine increased the T1 from 88.2% to 98.1% of the final T1 (Neo + 15), and the T4:T1 ratio increased from 0.51 to 0.97. When the initial TOF ratio was 0.9 the first dose of neostigmine did not alter the height of T1 and the T4:T1 ratio was increased from 0.94 to 1.02. There was no significant difference from Neo + 5 onwards in the height of T1 between the groups reversed from a TOF ratio of 0.5 or from greater than 0.9, and no significant changes over time were seen. The T4:T1 ratio showed significant differences between the groups ($p = 0.02$), and significant changes for both groups over time ($p = 0.005$).

Measurements of MMG TOF (Figures 5 and 6)

With the first dose of neostigmine the T1 increased from

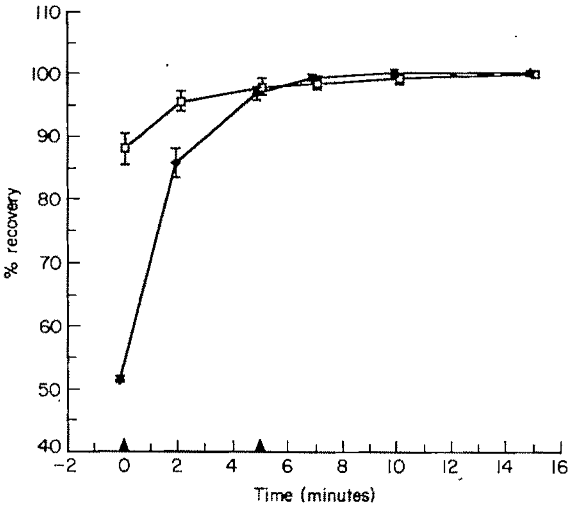

Fig. 3. Mean (SEM) of EMG T1 and T4:T1 when first dose of neostigmine administered at an EMG TOF ratio of 0.5. $n = 18$. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, EMG T1; —◆—, EMG T4:T1.

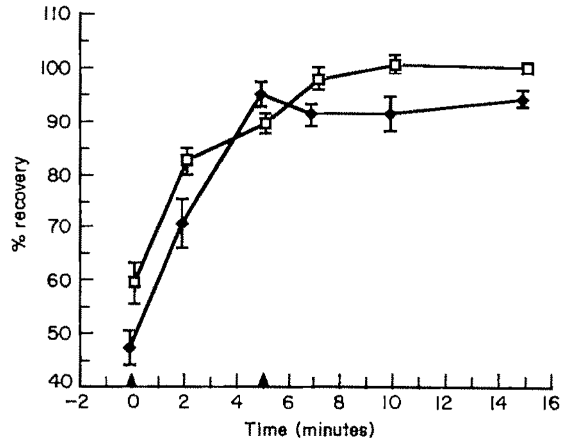

Fig. 5. Mean (SEM) of MMG T1 and T4:T1 when first dose of neostigmine administered at an EMG TOF ratio of 0.5. $n = 8$. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, MMG T1; —◆—, MMG T4:T1.

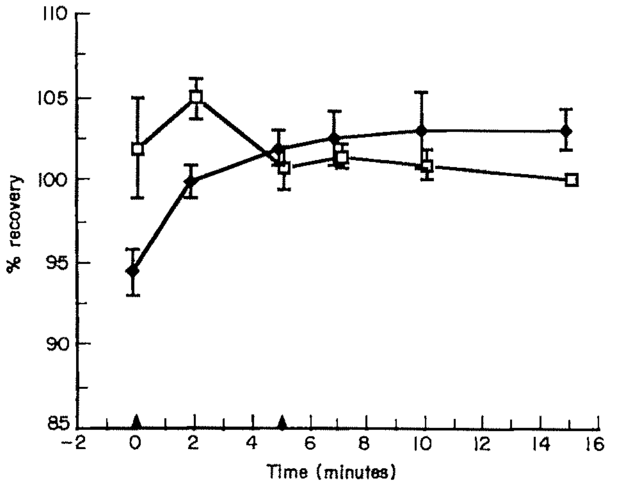

Fig. 4. Mean (SEM) of EMG T1 and T4:T1 when first dose of neostigmine administered at an EMG TOF ratio of 0.9. $n = 10$. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, EMG T1; —◆—, EMG T4:T1.

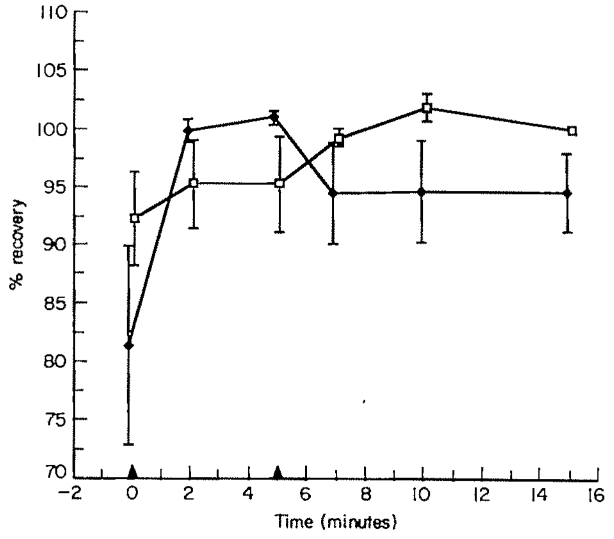

Fig. 6. Mean (SEM) of MMG T1 and T4:T1 when first dose of neostigmine administered at an EMG TOF ratio of 0.9. $n = 5$. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, MMG T1; —◆—, MMG T4:T1.

59.6% to 89.4% and the T4:T1 ratio from 0.47 to 0.95 in patients starting from a TOF ratio of 0.5. Those patients who started from a TOF of greater than 0.9 had an increase in T1 from 92.3% to 95.2% and of the TOF ratio from 0.81 to 1.01. There were significant changes over time ($p < 0.0005$) for the T1 from Neo + 5 onwards in both groups. There were no significant differences between the groups, or between the changes in each group over time. The T4:T1 ratio changed over time for both groups ($p = 0.05$), and there was no difference between the groups in this change over time. The decrease in the T4:T1 ratio from Neo + 5 to Neo + 7 was not significant in either group.

Measurements of MMG Tetanus (Figures 7 and 8)

In patients reversed at a TOF ratio of 0.5, the first dose of neostigmine increased peak tetanic tension to a maximum of 112.9% and the tetanic fade improved from 60.2% to 96.5% of peak height. In the other group peak tetanic height increased from 92.9% to 108% with the first dose, and tetanic fade was virtually abolished. From Neo + 5 onwards the peak tetanic height (Tt) for both groups showed significant changes over time ($p < 0.0005$), and the difference between the groups in the changes over time were also significant ($p < 0.0005$). There were significant differences in the Tp:Tt ratios for the two groups ($p = 0.02$), in changes over time ($p < 0.0005$), and between the two groups over time ($p < 0.0005$). The decrease in Tt from Neo + 5 to Neo + 7 was significant for both the patients reversed from a TOF ratio of 0.5 ($p = 0.005$), and those reversed from 0.9 ($p = 0.001$). The decreases at these times for the Tp:Tt ratio were also significant ($p = 0.03$ for reversal from a TOF ratio of 0.5, and $p = 0.003$ for reversal from 0.9).

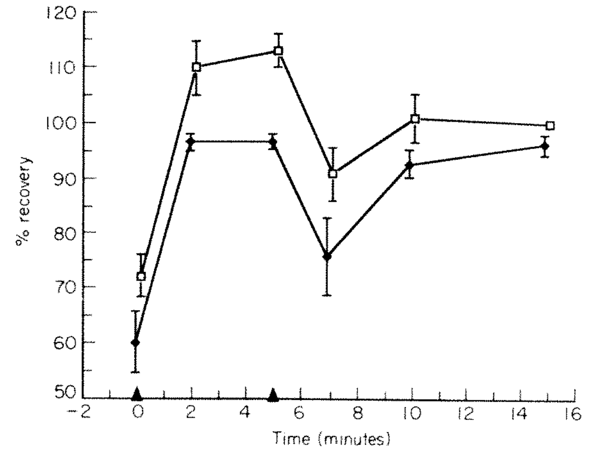

Fig. 7. Mean (SEM) MMG peak tetanic height (Tt) and tetanic fade over peak height (Tp/Tt) when first dose of neostigmine administered at an EMG TOF ratio of 0.5. *n* = 8. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, Tt; —◆—, Tp/Tt.

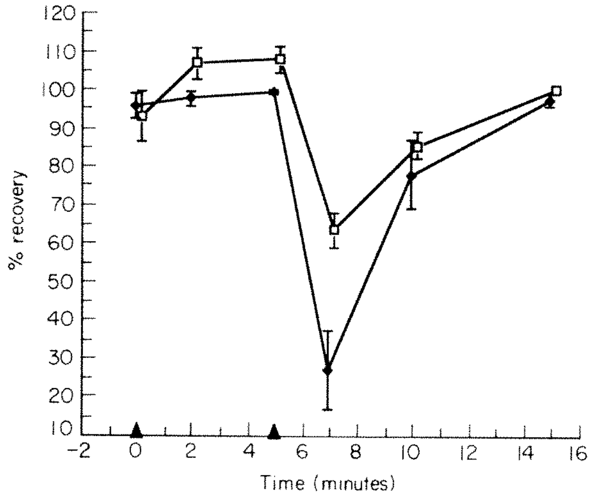

Fig. 8. Mean (SEM) MMG peak tetanic height (Tt) and tetanic fade over peak height (Tp/Tt) when first dose of neostigmine administered at an EMG TOF ratio of 0.9. *n* = 5. ▲, neostigmine 2.5 mg + atropine 1.2 mg. Height of T1 is presented as percentage of height at 15 minutes. —□—, Tt; —◆—, Tp/Tt.

In addition to the patient who did not receive any muscle relaxant, fasciculations were noted in one further patient who was reversed after spontaneous recovery to a TOF ratio of 0.9 had occurred. There was no evidence of muscle weakness in any patient during the recovery period, and the postoperative course was normal in all cases.

Discussion

It is considered standard practice in the United Kingdom to attempt antagonism of a non-depolarising neuromuscular blockade with a dose of neostigmine 2.5 mg, possibly followed by a second dose.[9] With the introduction of the newer medium-duration relaxants, atracurium and vecuronium, and the prospect of even shorter acting agents,[10] the possibility exists of administering neostigmine after muscle power has recovered spontaneously. It has been suggested that neostigmine may adversely affect muscle power in these circumstances.[1-3] The ability of neostigmine to cause a neuromuscular block has been described previously,[4] and this can be seen clinically after poisoning with anticholinesterase compounds,[11] in myasthenics in cholinergic crisis,[12] and in patients with neuromuscular disorders.[13]

It is thought that twitch tension depression and fade are the result of different mechanisms. The depression of twitch tension can be explained by simple block of postjunctional receptors.[14] The tetanic fade may be caused either by agents decreasing mobilisation of transmitter, or by the effects of tetanic stimulation increasing the frequency of ion channel opening, allowing drugs that block the channels increased access.[14] Our results show that excess neostigmine has little effect on either the T1 or the T4:T1 ratio when using TOF stimulation, while with tetanic stimulation both twitch tension and fade are adversely affected.

The situation we have investigated is complex. Firstly the residual atracurium may occupy a large percentage of receptors even when tests of neuromuscular function show no muscle weakness.[15] Secondly neostigmine may potentially cause a neuromuscular block in a number of ways, and it is possible that a combination of mechanisms may account for the events we recorded.[14,16] The increase in acetylcholine available in the synaptic cleft may cause a depolarising block associated with fasciculations such as we observed.[4,17] The acetylcholine may also act at receptors on the prejunctional membrane and first node of Ranvier,[14,17,18] and thus affect nerve transmission or enhance a negative feedback mechanism which inhibits transmitter release. This is one of the explanations for the fade seen with anticholinesterase agents.[14] Other means by which a cholinesterase inhibitor may adversely affect muscle power include receptor channel blockade,[14,17,19] which may also cause tetanic fade. In addition relatively little acetylcholine will be broken down in the synaptic cleft, possibly decreasing the amount of choline being taken up into the nerve terminal to take part in the manufacture of more acetylcholine. This may result in diminished stores of readily available transmitter. Patients also vary in the amount of cholinesterase they possess, and therefore possibly in the effect of a given dose of neostigmine. Finally, it may not be realised that the atropine given with the neostigmine may itself, in certain circumstances, affect neuromuscular transmission.[4,19,20]

The potential risk of neostigmine lies in its ability to cause muscle weakness, and thus affect breathing, coughing and the patency of the airway. Assessment of this is ideally clinical, but requires the cooperation of an awake and attentive patient. Several methods of stimulating the ulnar nerve and measuring muscle power or EMG have been developed in order to assess muscle power under anaesthesia. The method of TOF stimulation has gained wide popularity, and a TOF ratio of 0.7 to 0.8 was shown to correlate with signs of clinical recovery.[6] These ratios are broadly accepted, but in the case of atracurium a TOF ratio of 0.5 may be sufficient.[21] Other forms of stimulation have also been used, including tetanic impulses of different durations and frequency.[6,22,23] We chose to use three different measures; the TOF measured electromyographically and mechanomyographically, and a one-second tetanus. The tetanic stimulation was used since it correlates well with maximum voluntary effort,[6] is sustained in the absence of muscle relaxants,[24] and was the method previously used when describing this problem.[2] We confirmed that the spontaneous recovery from tetanic fade occurs faster than TOF fade[23] (Table 1). However, the adverse effect of neostigmine on neuromuscular function was primarily seen with tetanic stimulation. This form of stimulation is said to be more physiological[8] and may be a more important indicator than TOF monitoring in the circumstances we investigated.

The EMG did not show any adverse effects of the neostigmine, and this has been seen in similar circumstances by others.[25] The EMG solely reflects changes in excitable membranes, whereas mechanomyography is also affected by changes in excitation–contraction coupling and the contraction of the muscle.[22] The changes that we observed with mechanical measurements may reflect a direct depressant effect of the neostigmine on muscle fibres. In support of this theory Kawabuchi showed in rats that neostigmine can cause a calcium ion mediated myopathy which may not be reflected on the EMG.[26] Edrophonium has been shown to have no effect on tetanic fade in patients who had a considerable degree of spontaneous recovery of neuromuscular blockade.[1] This may indicate that the block we saw is at least partly specific to neostigmine, and is not totally related to the increase in acetylcholine at the neuromuscular junction.

There have been previous reports of neostigmine given to subjects who had not received muscle relaxants.[2,27,28] We therefore felt it was acceptable to repeat this experiment which models the situation where spontaneous recovery from a relaxant has continued to the point where no relaxant remains in the vicinity of the receptor. Our case confirms that important decreases in monitored muscle power occur. However these changes were only marked after the second dose of neostigmine, and recovered spontaneously within a relatively brief period. Previous work has confirmed this, as well as indicating that divided doses of neostigmine cause more fade than a single dose of the same amount.[2] Payne *et al.* did not report fasciculations in their patients. Fasciculations similar to those reported here were previously decribed,[4,28] but we decided not to continue with further subjects.

Different methods of assessment of neuromuscular blockade and recovery, although in broad agreement, measure different things.[22] It is therefore not surprising that in some cases the results differ. The MMG recordings with tetanic stimulation showed the most marked effect after the neostigmine. With all the methods of measurement, whether the degree of spontaneous recovery was a TOF ratio of 0.5 or 0.9, a first dose of neostigmine 2.5 mg showed no evidence of causing a decrease in muscle power. There was in all cases either some recovery of measured neuromuscular function, or no change. The second dose of neostigmine 2.5 mg monitored using tetanic stimulation caused a decrease in evoked neuromuscular function. In no case did the TOF ratio fall below the widely accepted figure for recovery of 0.75. The change in tetanic contraction was marked, but recovery took place within a short time. It is reasonable to conclude that even when considerable spontaneous recovery of muscle power has occurred, a single modest dose of reversal agent is unlikely to cause clinically important muscle weakness, and any effects are probably short lived.

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Anaesthesia, 1989, Volume 44, pages 300–302

Rebreathing during spontaneous and controlled ventilation with T-piece breathing systems: a general solution

K. L. DORRINGTON AND J. R. LEHANE

Summary

A general solution is presented to the problem of finding the degree of rebreathing generated by T-piece breathing systems. The solution is applicable to any ventilatory waveform, dead space volume and tidal volume and is identical for spontaneous and controlled ventilation for any given ventilatory waveform. The method is graphical and its use and understanding require no mathematical skills. However, if an analytical form of the ventilatory waveform is known, the method is easily extended by use of calculus to obtain a precise analytical solution.

Key words

Equipment; breathing systems, T-piece, Bain.
Complications; rebreathing.

T-piece systems are the most commonly used rebreathing systems for patients who have controlled ventilation during anaesthesia, and are frequently used during spontaneous ventilation. A co-axial form of T-piece system has been recommended as a universal breathing system.[1] However, there remains no satisfactory general analysis of its function, despite its widespread use.[2]

Theoretical modelling of the rebreathing characteristics of T-piece systems is made difficult by the variability of ventilatory waveforms and the size of the dead space (V_D) in relation to the tidal volume (V_T). Mapleson[3] adopted a square-wave flow-time ($\dot{V}$–t) waveform. Onchi *et al.*[4] chose a sinusoidal waveform. Willis *et al.*[5] modified a simple sinusoid to allow for different inspiratory and expiratory times. Other authors have used a theoretical model which takes no account of the influence of ventilatory waveform on rebreathing.[6,7]

The picture is complicated by the widespread practice of describing[8,9] and summarising[10,11] the function of T-piece systems under the separate headings of spontaneous and controlled ventilation. This paper shows that for a given ventilatory waveform the performance of a T-piece during spontaneous ventilation is identical to its performance during controlled ventilation, and that a single analysis is sufficient. Differences in fresh gas flow requirements in the two situations arise because of differences in the amplitude and shape of the ventilatory waveforms encountered.

The shape of the ventilatory waveform is important; that it determines the behaviour of T-piece systems has recently been emphasised in theoretical,[12] laboratory,[13] and clinical,[14] studies. We present a general solution to the problem of calculating rebreathing in T-piece systems. The solution is 'general' in that it applies to all ventilatory waveforms, for all values of V_D/V_T, during either spontaneous or controlled ventilation.

We have previously shown[12] that, by depicting spontaneous ventilation as a plot of volume (V) against time (t), the fresh gas flow which prevents rebreathing can be determined from simple graphical constructions for all systems in the Mapleson classification A to E. The same V–t plot is used here to determine the extent of rebreathing with T-piece systems during both spontaneous and controlled ventilation.

Theoretical assumption

The analysis makes the usual assumption that there is no axial mixing (dispersion) of gases within the ducts of the breathing system. This represents a limitation to the practical application of the results of this and the preceding analyses referred to above. The percentage error which arises by neglecting axial mixing is very large with high frequency ventilation, but is unlikely to exceed 20% with normal modes of ventilation.[15]

The solution presented here is a precise corollary of this assumption of absent axial mixing, so comparison of this theory with laboratory and clinical measurements could represent a direct measure of the extent to which axial

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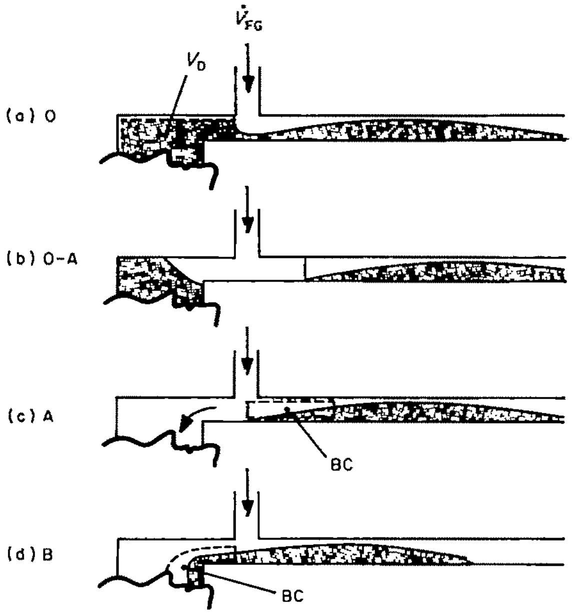

Fig. 1. Structural components common to all T-piece systems represented at four stages in the ventilatory cycle depicted in Figure 2. Expired alveolar gas is shaded. $\dot{V}_{FG}$ is the fresh gas flow, V_D the anatomical and equipment dead space volume.

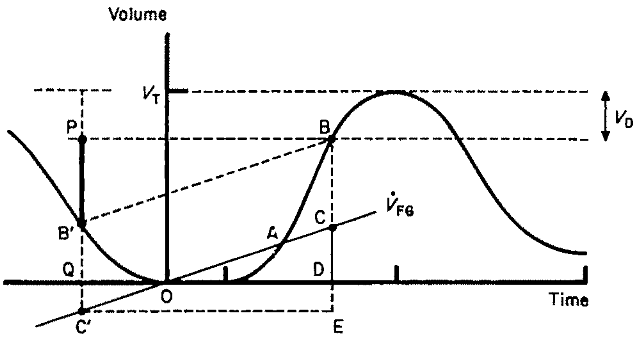

Fig. 2. Ventilatory waveform with construction which depicts the volume of gas PB′ which contributes to effective alveolar ventilation during a breath of inspired tidal volume V_T, with either spontaneous or controlled ventilation using a T-piece system. Lines B′B and C′C have a slope which is equal to the fresh gas flow $\dot{V}_{FG}$.

mixing contributes to gas exchange in T-piece systems. Previously this has not been possible for the general case of any ventilatory waveform.

Theoretical analysis

Figure 1(a–d) depicts the components which are common to all T-piece systems in general use. Fresh gas enters with a steady flow at a T, one branch of which joins a reservoir tube and the second connects to a dead space of volume V_D. V_D is the sum of the anatomical dead space and equipment dead space, but is represented in Figure 1 as the volume within a facemask. The following behaviour can be deduced regardless of whether ventilation is spontaneous, manually controlled from a reservoir bag, or automatically controlled by a ventilator at the end of the reservoir tube which is remote from the patient. (We assume that the volume of the reservoir tube is sufficiently large to prevent gas from the reservoir bag or the ventilator from reaching the alveoli.)

The dead space contains gas which was breathed out from the alveoli (Fig. 1a) immediately after completion of an expiration. The reservoir tube contains a mixture of expired and fresh gas, which is stratified along the tube according to the relative flows with which these two constituents arrive at the T-piece throughout expiration. It is assumed that mixing occurs at right angles to the long axis of the tube, but the expired alveolar gas and fresh gas are represented as distinct, respectively as shade and clear in Figure 1. Figure 2 is a plot of the ventilatory waveform labelled in relation to Figure 1(a–d). The origin of the plot ($V = 0$, $t = 0$) is taken to be at the end of an expiration. Inspiratory flow does not necessarily start at the origin since there may be a pause between expiration and inspiration.

The volume of gas expired is usually closely equal to the volume of gas inspired, and so the V–t plot often falls back to touch the horizontal axis at the end of expiration. Differences between inspired and expired volumes do occur, as a result of uptake or elimination of anaesthetic gases, but this does not affect the analysis presented here. The fresh gas flow ($\dot{V}_{FG}$) is represented on a V–t plot by a straight line which passes through the origin and has a slope equal to $\dot{V}_{FG}$.

Early in inspiration fresh gas accumulates at the patient end of the reservoir tube (Fig. 1b). This is because the inspiratory flow is initially less than the fresh gas flow. At moment A, which is depicted in Figures 1c and 2, the volume of fresh gas which has arrived since the end of expiration exactly equals the volume of gas which has entered the alveoli. A line of slope $\dot{V}_{FG}$ which passes through the origin cuts the inspiratory limb of the waveform at this point. At this moment some CO_2-containing gas from the reservoir tube enters the dead space. All such gas which enters the dead space before point B in Figure 2 will be inspired into the alveoli. This point lies a vertical distance V_D below the peak of the waveform. Gas which enters the dead space after point B will not reach the alveoli, and is consequently of no functional significance.

It follows that the gas which enters the alveoli can be divided into two components represented by CD and BC. CD represents the volume of fresh gas delivered to the system since the end of the previous expiration. BC represents the volume of CO_2-containing gas which is derived from the reservoir tube. In fact BC is a mixture of fresh and alveolar gas which were delivered to the reservoir tube during the latter part of the previous expiration.

The ratio of alveolar gas to fresh gas in this component BC can be derived as follows. A line of slope $\dot{V}_{FG}$ is constructed from point B to cut the preceding expiratory curve at B′. This line is parallel to OC. Line OC is projected leftwards to C′ which lies vertically below B′. B′C′ (= BC) represents the total volume of CO_2-containing gas from the reservoir tube which enters the alveoli. Of this, volume QC′ is the fresh gas delivered during expiration, while volume B′C′ was accumulating in the reservoir tube. The remaining component B′Q is that part of B′C′ which is alveolar gas. The total volume of fresh gas which is delivered between points C′ and E is represented by CE (= PB′) and represents the volume of gas which contributes to the effective alveolar ventilation ($\dot{V}_{A\text{eff}}$).

$$\dot{V}_{A\text{eff}} = \frac{\text{PB}'}{t_B} \qquad (1)$$

where t_B is the time for one breath.

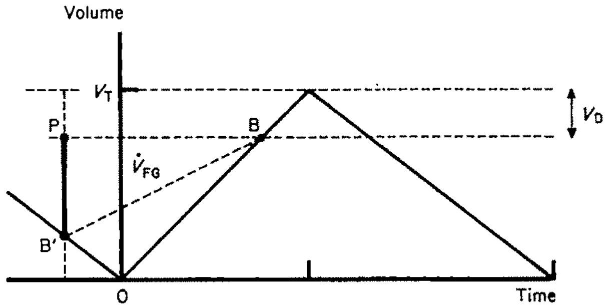

Fig. 3. The equivalent construction to the triangle BB′P in Figure 2 for a ventilatory waveform which consists of constant inspiratory and expiratory flows.

In its simplest form the construction involves the following manoeuvre: point B is located on the inspiratory limb of the V–t curve as the point where a volume $V_T - V_D$ has been inspired. A line of slope $\dot{V}_{FG}$ is drawn through B. This intersects the expiratory curve of the previous breath at B′. The vertical distance between B and B′ is the contribution towards $\dot{V}_{A\text{eff}}$.

The solution for a triangular V–t waveform

A simple respiratory waveform (Fig. 3) is one in which there is a constant inspiratory flow and a constant expiratory flow. On a flow-time ($\dot{V}$–t) plot this constitutes the square wave ventilatory flow waveform analysed by Mapleson.[3] The graphical construction applied to this waveform is shown in Figure 3.

B′ is located as the intercept of a line of slope $\dot{V}_{FG}$ through point B, and the expiratory limb of the V–t curve for the preceding breath. Line PB′ represents the volume of fresh gas which reaches the alveoli during inspiration of a volume V_T. This simple analysis generates an identical result to the analytical analysis of Mapleson.[3]

Effects of end expiratory pause and different inspiratory and expiratory volumes

The presence of an end expiratory pause or of unequal inspiratory and expiratory volumes does not invalidate the analysis. Both are depicted as present in Figure 2.

Effect of irregularity of breathing

The analysis makes no assumption about the regularity of breathing. The V–t waveforms for sequential breaths are permitted to vary in both shape and amplitude. However, equation 1 for any one breath will become valid as a mean over any length of time if breathing is regular.

Elimination of rebreathing

We define rebreathing as the inhalation into the alveoli of a volume of gas that contains carbon dioxide in addition to the gas which is present in the dead space at the time inspiration commences. Figure 2 shows that rebreathing can be eliminated only if point A coincides with point B. The graphical construction then reduces to that which has already been published.[12]

Spontaneous versus controlled ventilation

We emphasise that the performance of T-piece systems for a given amplitude and shape of ventilatory waveform is identical during spontaneous and controlled ventilation. Different fresh gas flow requirements during the two situations arise either from differences in amplitude, or in the shape of the waveform. For example it is common practice with controlled ventilation using these breathing systems to combine rebreathing with hyperventilation so as to obtain an appropriate effective alveolar ventilation as defined by equation 1.

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Bradycardia in patients receiving atracurium or vecuronium in conditions of low vagal stimulation

D. A. COZANITIS, L. LINDGREN AND P. H. ROSENBERG

Summary

Four groups of 20 patients each received either vecuronium or atracurium together with either glycopyrronium or saline, and underwent anaesthesia free of vagolytic drugs, and surgery devoid of vagal activity. Determinations of plasma histamine concentrations were made to examine the possible correlation between these levels and changes in heart rate and blood pressure as well as a possible relationship with skin reactions after the administration of the relaxants. Patients who received vecuronium without the anticholinergic drug, glycopyrronium, showed a greater tendency towards bradycardia (though not statistically significant) than those given atracurium. More cutaneous reactions were observed with patients who received atracurium than in those with vecuronium, but there was no correlation with plasma histamine concentrations of either relaxant group. There was no correlation either between histamine concentrations and heart rate or blood pressure associated with atracurium. The incidence of bradycardia with either relaxant is low if the anaesthetic technique and the surgery are devoid of vagal activity.

Key words

Complications; bradycardia.
Neuromuscular relaxants; atracurium, vecuronium.

The incidence of intra-operative bradycardia is significantly higher when vecuronium, rather than pancuronium, is used as muscle relaxant. The occurrence of bradycardia was markedly reduced when glycopyrronium was given at the induction of anaesthesia.[1] Some of the patients in that study had surgery whose nature could provoke vagal activity, e.g. genital or abdominal operations. In addition, fentanyl, a drug with high vagotonic activity, was included in the anaesthetic technique. We therefore decided to examine the bradycardia associated with vecuronium but to exclude these two variables.

Atracurium was also studied because, like vecuronium, it lacks vagolytic activity and was associated with intra-operative bradycardia.[2] A high incidence of skin reactions after atracurium was noted and it is postulated that these result from histamine release.[3,4] It is possible that the release of histamine may elicit haemodynamic changes, so in the present study, plasma histamine concentrations were also measured.

Methods

Eighty adult male and female patients, ASA grades 1 and 2, with a maximum weight of 80 kg and aged less than 70 years, undergoing varicose vein or breast surgery were studied after approval of the hospital ethics committee. The presence of cardiovascular disease, concomitant administration of drugs with known cardiovascular activity, and ECG abnormalities were exclusion factors.

The patients were seen and their verbal consent was obtained at noon on the day before surgery. They received chlordiazepoxide 5–20 mg in two oral doses that afternoon and nitrazepam 5–10 mg was given at night. Forty-five minutes before the start of anaesthesia the patients were given, intramuscularly, oxycodone 0.12–0.14 mg/kg (maximum 10 mg) and diazepam 5–10 mg orally.

Allocation was at random into four study groups of 20 patients each, depending upon the relaxant and the intravenous pre-induction anticholinergic agent, as follows: Group 1, vecuronium–glycopyrronium; Group 2, vecuronium–saline; Group 3, atracurium–glycopyrronium, and Group 4, atracurium–saline.

An intravenous infusion of warmed Ringer's solution was established in the operating room and, in the contralateral arm, a cubital vein was cannulated. The patients received, under randomised double-blind conditions, an intravenous injection of either glycopyrronium or physiological saline in equal volumes after a period of oxygenation; the doses of glycopyrronium were related to the body weight as follows: $\leqslant 59$ kg, 0.20 mg; 60–74 kg, 0.25 mg; $\geqslant 75$ kg, 0.30 mg.

Thiopentone sodium 5 mg/kg was given to induce

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Table 1. Demographic and operative data of the patients studied. Standard deviation is given in brackets. There were 20 patients in each group.

	Group			
	1	2	3	4
Age, years	44	45	46	43
	(9)	(12)	(12)	(10)
Females, *n*	20	20	19	19
Weight, kg	61	62	64	64
	(8)	(9)	(8)	(5)
Height	164	163	164	164
	(6)	(4)	(5)	(6)
Breast operations, *n*	19	16	18	17
Duration of anaesthesia, minutes	119	126	119	115
	(57)	(51)	(53)	(44)

Table 2. Mean (SD) heart rates (beats/minute) of the four groups at various times of the study.

	Group			
	1	2	3	4
On admission	72	64	65	67
	(13)	(8)	(11)	(10)
One day before operation	82	74	74	73
	(12)	(8)	(10)	(6)
Before induction	74	67	71	70
	(13)	18	(20)	(15)
Before relaxant	81	73	80	74
	(14)	(18)	(15)	(14)
Before laryngoscopy	86	71	81	74
	(13)	(15)	(10)	(9)

Table 3. Mean (SD) lowest heart rate, need for atropine and lowest individual heart rate.

	Group			
	1	2	3	4
Means lowest heart rate	64	54	62	55
	(9)	(9)	(5)	9
Need for atropine	1/20	4/20	0/20	1/20
Lowest heart rate	42	42	51	45

Table 4. Plasma histamine concentration [nmol/litre, mean (SD)] before anaesthesia and 2 and 5 minutes after relaxant.

	Group			
	1	2	3	4
Before induction	10	5	11	8
	(11)	(6)	(14)	(10)
2 minutes after relaxant	9	4	11	7
	(9)	(6)	(14)	(8)
5 minutes after relaxant	8	11	8	5
	(9)	(13)	(8)	4

anaesthesia. Either vecuronium 0.1 mg/kg or atracurium 0.5 mg/kg was injected rapidly when the eyelash reflex was lost; allocation to either of these two relaxants was random and the administration double-blind. Oxygen–nitrous oxide (1:1) was delivered to the patients through a mask and end-tidal carbon dioxide concentration monitored to maintain normocapnia. Neuromuscular monitoring using the train-of-four technique was started and, when only one twitch remained, the trachea was intubated. Anaesthesia was maintained with O_2/N_2O (1:2) and enflurane. When two twitches of the train-of-four returned, increments of 0.25 of the original dose of relaxant were injected. The presence of skin reactions after the injection of the relaxant was recorded. Heart rate and blood pressure were recorded at regular intervals throughout anaesthesia using an oscillotonometer.

Atropine 1.0 mg was always available in a syringe, and patients received 0.5 mg when the anaesthetist felt that the clinical situation required it. Venous blood was withdrawn before induction of anaesthesia and at 2 and 5 minutes following the initial dose of relaxant. Plasma histamine concentration was measured according to the method of Dyer *et al.*;[5] the normal range of plasma histamine in this hospital is 0–7 nmol/litre.

Heart rate and blood pressure data were analysed using the two sample *t*-test. The binomial data were analysed with the Chi-squared test.

Results

Details of the patients studied are shown in Table 1; they were well matched.

Table 2 shows that the mean heart rates immediately before induction of anaesthesia, i.e. after premedication, were very similar to those recorded beforehand. Those patients who were given glycopyrronium (Groups 1 and 3) during the interval from before administration of the relaxant to before laryngoscopy had mean heart rates which were slightly more rapid than those of patients who had saline (Groups 2 and 4) $p = 0.057$. All groups apart from Group 4, had mean heart rates before the injection of the relaxant which were significantly higher than those of the period before induction ($p < 0.004$ to < 0.02).

The mean systolic and diastolic blood pressures did not differ significantly between the groups at any of the times studied. Atropine was needed in one patient given glycopyrronium (Table 3). By contrast, five of the 40 individuals who received saline required atropine; four of these received vecuronium; one atracurium, ($p > 0.17$). Six of the 40 patients (15%) who had vecuronium, and 16 (40%) of the patients who had atracurium displayed flushing over the upper chest, ($p < 0.025$). Independently or together with flushing, wheals and flares appeared in 14 and two of the patients respectively in the atracurium and vecuronium groups, $p < 0.001$. The wheals and flares were predominantly found on the hand or arm of the injection site; however, they were also noted on the back of one patient and on the opposite arm of another.

The mean plasma histamine concentrations of the study groups are seen in Table 4. The concentrations were above the normal range before the induction of anaesthesia, except for Group 2 (vecuronium–saline). There was neither consistent change in mean concentration, nor was there any measurable relationship between change in heart rate and change in plasma histamine concentrations.

Discussion

The incidence of the need for atropine during the use of vecuronium in an anaesthetic technique which included fentanyl and surgical procedures capable of invoking vagal stimulation was 48% ($n = 25$) in a previous study.[1] Both of these factors were excluded in the present study and the incidence was lower, 20% ($n = 20$). This finding adds strength to the suggestion that vecuronium-associated bradycardia is a result primarily of vagal stimulation rather than the vecuronium *per se*. On the other hand, the fact that the incidence of bradycardia was higher than that observed in the group that received atracurium, despite identical anaesthesia and surgery, does not rule this out completely. It appears that small doses of the anticholinergic drug glycopyrronium, which do not significantly alter heart rate during operation, can reduce the incidence of bradycardia associated with the use of these two relaxants.

The lack of significant change in heart rate and blood pressure in the groups of patients who have atracurium is in accordance with that reported earlier;[6,7] although other workers found hypotension and an increase in heart rate after atracurium 0.6 mg/kg, the changes did not correlate with plasma histamine levels.[8]

The incidence of skin flushing after atracurium and vecuronium is similar to that noted earlier.[4] There were significantly more patients with skin reactions in the groups who had atracurium, but this was not accompanied by an increase in plasma histamine concentrations. Likewise, there were patients with increases in plasma histamine concentrations who did not exhibit concomitant cutaneous manifestations. Interestingly, the only group that showed an increase in plasma histamine concentration from the second to the fifth minute after the relaxant was the vecuronium–saline group.

The incidence of clinically significant bradycardia in patients who receive vecuronium or atracurium is low, provided that the anaesthetic technique is free from vagotonic agents, and the surgery devoid of vagal stimulation.

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Anaesthesia, 1989, Volume 44, pages 306–309

The value of postoperative chest radiology after major abdominal surgery

M. H. COOPER AND J. N. PRIMROSE

Summary

A prospective study was carried out in which a chest radiograph was performed routinely on the third postoperative day on 35 consecutive patients who had elective abdominal surgery. The aim was to determine whether clinical symptoms and signs could be correlated with the radiographic appearances and whether the routine use of such an X ray could detect serious chest pathology before clinical signs developed. Thirteen patients (37%) had radiological evidence of complications and all had symptoms and (or) signs which suggested postoperative chest pathology. The 22 patients (63%) who had no radiological abnormality, could be subdivided clinically into those who were normal (29%) and those who had symptoms and (or) signs (34%). There was no significant difference between the groups in terms of previous surgery, sex, smoking, nature of surgical incision, age or duration of anaesthesia. There was a poor correlation between the diagnosis of the chest abnormality detected clinically and the diagnosis suggested by the radiographs. These findings suggest that a routine postoperative chest X ray is unnecessary in the absence of clinically detectable chest pathology.

Key words

Complications; postoperative respiratory morbidity diagnosis, X ray.
Surgery; abdominal.

Postoperative chest problems are common after abdominal surgery. These problems are frequently termed 'chest infection' on the basis of symptoms and signs detected clinically and, although a chest X ray is frequently performed at this stage, treatment is usually instituted regardless of the result. Relatively few published studies have attempted to compare the symptoms and signs detected in patients with the changes to be found in postoperative chest radiographs, although Hamilton *et al.*[1] had found some degree of inconsistency between chest X rays, clinical observations and blood gas analyses in patients with pulmonary collapse. The frequency of postoperative pulmonary complications and the morbidity and even mortality that they cause, makes this an important problem to address.

This study aimed to test the hypothesis that a routine postoperative chest radiograph would reveal relevant pulmonary complications before the development of clinical symptoms and signs. These complications, accurately diagnosed, could therefore be treated with appropriate therapy.

Table 1. Operative procedures in 35 patients.

Operation	n (%)
Transverse or sigmoid colectomy	14 (40)
Anterior resection	2 (6)
Abdominoperineal resection	4 (11)
Abdominal rectopexy	1 (3)
Highly selective vagotomy	1 (3)
Cholecystectomy	13 (37)

Patients and methods

Thirty eight consecutive patients who had major elective abdominal surgery were studied. The respiratory status was established before operation on the basis of clinical examination, and by questions related to chest symptoms and lifestyle, taken from the Medical Research Council Respiratory Assessment Protocol.[2] This is a set of standardised questions which enables the diagnosis and severity of the chest disease to be assessed. It was established, on the basis of the examination and standardised questions, that two patients suffered from well controlled asthma, two from chronic bronchitis and

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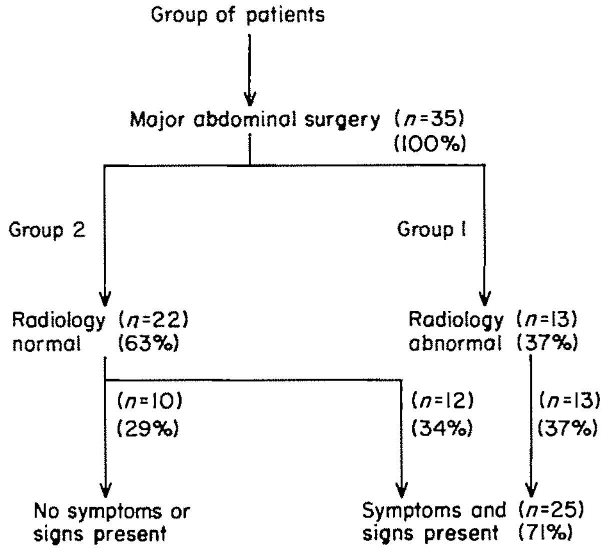
Group of patients
Major abdominal surgery (n=35) (100%)
Group 2
Group 1
Radiology (n=22) normal (63%)
Radiology (n=13) abnormal (37%)
(n=10) (29%)
(n=12) (34%)
(n=13) (37%)
No symptoms or signs present
Symptoms and (n=25) signs present (71%)

Fig. 1. Summary of results of present study.

Table 2. Clinical features exhibited in Groups 1 and 2.

Clinical feature	Group 1 n = 13	Group 2 n = 22
Pyrexia	8	12
Chest signs	13	10
Sputum production	4	10

Table 3. Correlation of clinical and radiological features in Group 1 patients (13).

	Radiological feature			
Clinical feature	Collapse n = 3	Infection n = 4	Pleural effusion n = 4	Pleural effusion and collapse n = 2
Pyrexia	3	4	0	1
Chest signs	3	4	4	2
Sputum production	1	3	0	0

Table 4. Pre-operative and operative variables in Groups 1 and 2.

Clinical feature	Group 1	Group 2
Males:females	5:8	9:3
Previous history of respiratory disease	3	3
Smokers	8	13
Previous surgery	7	12
Surgery		
Upper abdominal	8	5
Lower abdominal	2	7
Upper and lower abdominal	3	10

the remaining 31 patients were classed as normal.

Patients received physiotherapy postoperatively which consisted of twice daily 15-minute breathing exercises, with subsequent assisted coughing and intermittent percussion and vibration of the chest wall. The physiotherapy was started on the first postoperative day and continued for a further 4 days. Patients received postoperative analgesia in the form of parenteral opiates.

Clinical assessment

Patients were assessed daily for 5 days in the postoperative period, by a single observer, and their symptoms and (or) signs recorded. A clinical diagnosis was made of collapse, infection or pleural effusion where appropriate. Collapse was defined by production of mucoid sputum, chest signs of collapse and pyrexia. Infection was defined as pyrexia, production of purulent sputum and signs of chest infection. Sputum (where available) was sent for microscopy, culture and antibiotic sensitivity of any organism cultured. Prophylactic antibiotics were given both pre- and postoperatively; these were gentamicin (80 mg) and metronidazole (500 mg) in three doses for colonic surgery and cephradine (1 g) in three doses for gastric and biliary surgery.

Radiological assessment

Patients had a chest radiograph performed on the third postoperative day. Most patients were well enough to leave the wards; however, when this was not possible a ward film was requested. Reports on the films made by one Consultant Radiologist noted the presence of predefined radiological features:[3] consolidation, collapse and (or) pleural effusion on one or other side or a normal X ray [which included raised hemidiaphragm and (or) gas under the diaphragm].

The patients were subdivided into two groups; those who had abnormal radiology and those who did not. Pre-operative respiratory status, cigarette smoking habits, sex, previous surgery and the surgical incision used were compared using the Chi-squared test with Yates' correction. Age and duration of surgery were compared with a Mann-Whitney *U* Test.

Results

Two of the 38 patients who were included in the study were excluded at their own request postoperatively, and one because he had advanced malignancy and was terminally ill. There were 35 patients for assessment.

Ten patients (29%) had neither symptoms nor signs (Fig. 1). Thirteen patients (37%) had evidence of pulmonary complications as judged by radiological features alone, (Group 1). Four of these (11%) had a pleural effusion, four (11%) consolidation and three (8%) collapse, with an additional two patients (6%) who had evidence of both pleural effusion and collapse (Tables 2 and 3). The remaining 22 patients (63%) had no radiological abnormalities (Group 2). Twenty-five patients (71%) exhibited symptoms and (or) signs which were suggestive on clinical grounds of significant chest pathology.

The patients in Group 1 all had some clinical evidence of chest complication, whether this was pyrexia, production of sputum or specific chest signs (Tables 2 and 3). Of the 22 patients in Group 2 (Table 2), 12 patients (34%) were pyrexial, 10 (29%) had chest signs and 10 (29%) produced sputum. The patients in either Group 1 or Group 2 who produced sputum had no bacteriological evidence of respiratory pathogens. The sputum was purulent in 75% of Group 1 and 40% of the Group 2 specimens.

Table 5. Comparison of age and duration of anaesthesia between Groups 1 and 2.

	Group 1 Median (range)	Group 2 Median (range)	p
Age, years	73 (84–32)	66 (86–25)	0.251 (ns)
Duration of anaesthesia, minutes	110 (480–50)	133 (540–60)	0.295 (ns)

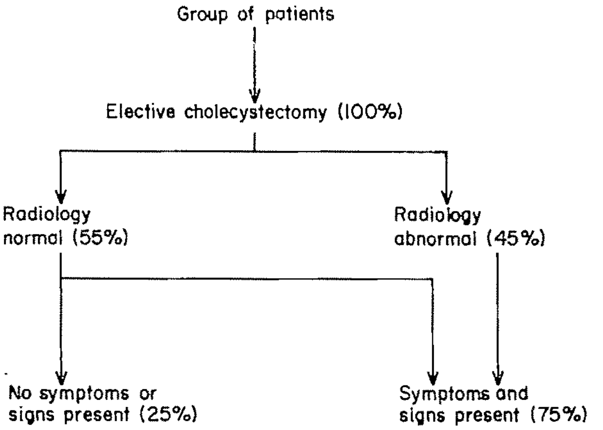
Group of patients
Elective cholecystectomy (100%)
Radiology normal (55%)
Radiology abnormal (45%)
No symptoms or signs present (25%)
Symptoms and signs present (75%)

Fig. 2. Summary of results of Hansen *et al.*[5]

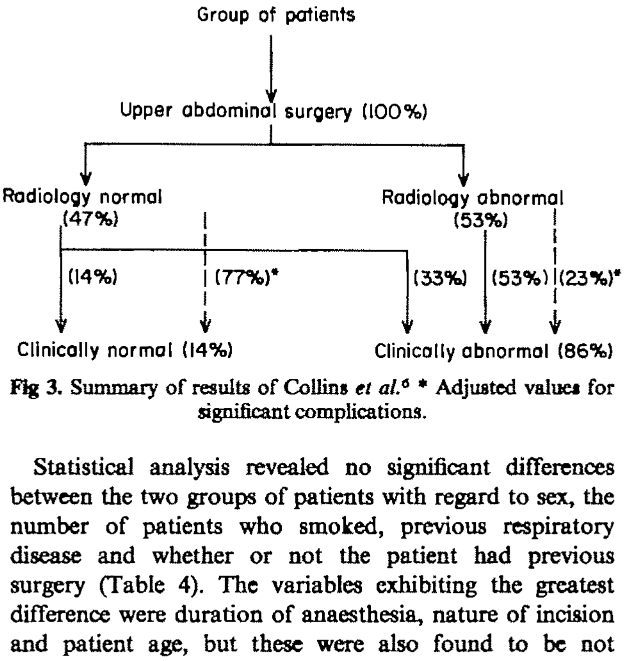

Fig 3. Summary of results of Collins *et al.*[6] * Adjusted values for significant complications.

Statistical analysis revealed no significant differences between the two groups of patients with regard to sex, the number of patients who smoked, previous respiratory disease and whether or not the patient had previous surgery (Table 4). The variables exhibiting the greatest difference were duration of anaesthesia, nature of incision and patient age, but these were also found to be not statistically significant (Table 5).

Discussion

This study has demonstrated that patients with radiological evidence of chest abnormality invariably had chest signs which were demonstrated clinically, although some patients with clinical signs had a normal chest radiograph. Patients who had radiological complications did exhibit varying combinations of symptoms and signs (Table 3). Pyrexia was found to be more suggestive of collapse or infection, as was sputum production, whilst chest signs were evenly distributed throughout the different radiological categories. It was rare for any of the patients in Group 1 to fit unequivocally on clinical grounds into a category of effusion, collapse or infection.

The lack of consistency between the chest and X ray findings requires some explanation. Clearly, the effects of observer variation, the pre-operative respiratory status and the actual operation performed may play a part. However, the principal explanation is that the postoperative chest condition changes rapidly in the first few days after operation and the chest radiograph provides only one 'picture' of the evolution of these changes. Goodman[4] has suggested that serial radiographs would be more useful in this respect.

Two other studies, in patients who had upper abdominal procedures, produced results which were similar to those of the present study. Hansen *et al.*[5] demonstrated that 45% of patients had an abnormal chest X ray and correspondongly abnormal clinical findings (Fig. 2). Collins *et al.*[6] observed that 53% of patients had both radiological and clinical abnormalities (Fig. 3). These authors attempted to distinguish those complications which they thought significant, either clinically or radiologically: they found a 23% incidence of significant complications; however, although they defined a significant complication clinically, they failed to do this radiologically.

The criteria used for defining a pulmonary complication in other studies are variable. Morran and McArdle[7] distinguish between collapse and infection by the differences in sputum production and subtle changes on a chest X ray performed 3 days postoperatively.

They noted a 50% and 44% incidence of chest complications in control and cotrimoxazole-treated patients respectively after elective cholecystectomy. Wightman[8] defined a postoperative pulmonary complication clinically, and found that only 11% of patients developed complications, although the surgery performed was much more variable and some procedures were relatively minor. Goodman[4], in contrast, who reviewed postoperative radiographic changes, reported a 40–70% incidence of collapse on the chest X rays taken on the second postoperative day.

Eleven percent of patients in our study had radiological evidence of infection, although in no patient was sputum culture positive for pathogenic organisms. The most probable reason for this is that the numbers were small and, in addition, all of the patients received prophylactic antibiotics. Patients with a chest infection diagnosed radiologically in other studies, had a positive suptum culture in 60%[9] and 40%[10] of cases respectively. Wilkinson *et al.*[11] showed a closer correlation between clinical and bacteriological results of infection. The patients, however, were not receiving antibiotics nor regular prophylactic physiotherapy, unlike those in the present study.

The use of the chest radiograph before operation is a topic of recent interest. The Royal College of Radiologists[12] reported that these X rays neither seemed to influence a surgeon's decision to operate, nor was there any evidence that such X rays would be of value as a baseline in patients with postoperative pulmonary complications after the work of Rees *et al.*[13] The usefulness of the subsequently proposed guidelines was confirmed by Fowkes *et al.*[14] The present study supports the selective use of the postoperative chest X ray. Three of the patients included in the study had radiography requested by the clinicians; each of these patients had clinical features in the chest and in each case alteration to the treatment was influenced by the radiography. However, in none of the other chest radiographs performed routinely would the result have influenced the management of the patient. A routine postoperative radiograph is thus not indicated after elective abdominal surgery. A policy of regular clinical examination is important to identify patients whose clinical management may be influenced by such radiography. It may be beneficial for the Royal College of Radiologists' guidelines to be formulated for the postoperative chest X ray on the basis of this and other future studies.

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Anaesthesia, 1989, Volume 44, pages 310–316

Cerebral effects of anaesthesia and hypothermia

H. STEPHAN, H. SONNTAG, H. LANGE AND H. RIEKE

Summary

Cerebral blood flow, cerebral oxygen and glucose consumption, and cerebral lactate and pyruvate release were measured; spectral analysis of the EEG was recorded in 10 male patients who had coronary artery bypass surgery. The measurements were taken to evaluate the effects of fentanyl–midazolam anaesthesia during normothermia and during hypothermic nonpulsatile cardiopulmonary bypass at 26°C venous blood temperature, when a temperature-corrected $Pa\text{CO}_2$*-value of 5.3 kPa was maintained. Anaesthesia with fentanyl 7 μg/kg and midazolam 200 μg/kg as induction doses, followed by infusions of fentanyl 0.15 μg/kg/minute and midazolam 3 μg/kg/minute, was characterised by a decrease in fast-wave activity and an increase in high-amplitude, slow-wave activity in the EEG. There was also a decrease in cerebral blood flow (38%), oxygen consumption (22%) and glucose consumption (25%), while lactate and pyruvate production remained unchanged. Hypothermia of 26°C venous blood temperature suppressed EEG almost completely and decreased oxygen and glucose consumption by a further 61% and 54%, respectively, with no changes in lactate and pyruvate production while cerebral blood flow increased by 145%. These results show that the effects of fentanyl–midazolam anaesthesia on cerebral metabolism are enhanced during hypothermic cardiopulmonary bypass while the influence of anaesthesia on cerebral blood flow is overshadowed by the practice of a temperature-corrected acid-base management.*

Key words

Anaesthesia; cardiac.
Anaesthetics, intravenous; fentanyl, midazolam.

Neurological disorders after cardiac operations that use cardiopulmonary bypass (CPB) are still frequent, in spite of improved surgical and anaesthetic techniques. Stroke occurs in 5.2% of patients who have coronary artery bypass grafting,[1] while transient neuropsychiatric complications seem to be even more common.[2] The reasons are still unclear, because many of the variables, such as temperature, viscosity of blood, solubility of blood gases, which influence cerebral homeostasis change during hypothermic CPB. Moreover, nonpulsatile CPB seems to affect metabolic regulation in the brain by interfering with the myogenic contractility of cerebral vessels.[3]

Today, most cardiac operations use hypothermic, nonpulsatile CBF with exogenous CO_2 added to the pump oxygenator, to maintain a temperature-corrected $Pa\text{CO}_2$ of approximately 5.3 kPa. However, it is known that this acid-base management leads to an uncoupling of flow and metabolism during hypothermia,[4,5] whereas maintaining a nontemperature-corrected $Pa\text{CO}_2$ of 5.3 kPa seems a better way to preserve CBF regulation,[5–7] and thus may be physiologically appropriate.[8–10] Variations in the results of diverse groups may also be because of different methods of measuring CBF and (or) anaesthetic techniques. Intravenous anaesthetics are known to lead to a dose-related depression of cerebral metabolism and blood flow,[11–13] while volatile anaesthetics such as halothane, enflurane and isoflurane also suppress metabolism but increase blood flow; this leads to an impaired autoregulation.[14,15]

Recently, Nussmeier *et al.*[16] observed a significantly lower incidence of neuropsychiatric complications in patients subjected to pharmacological EEG suppression with thiopentone during CPB, than in a control group of patients anaesthetised with fentanyl and diazepam alone.

No detailed studies about cerebral metabolism under hypothermic conditions have been performed in man up to now, so we examined the effects of hypothermia plus fentanyl–midazolam anaesthesia on cerebral haemodynamics and oxygen, glucose, lactate and pyruvate metabolism in patients who have coronary artery bypass grafting. The study was to decide whether a nonpulsatile CPB technique that maintains a temperature-corrected $Pa\text{CO}_2$ of about 5.3 kPa, in combination with anaesthetic management, is able to preserve aerobic cerebral metabolism.

We used the argon wash-in technique[17] for measuring CBF, a modification of the Kety–Schmidt method,[18] because it is a very reliable technique and also almost

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independent of haematocrit and temperature in the ranges which occurred in our study.

Methods

Ten male patients scheduled for elective coronary artery bypass surgery were studied. Their ages ranged from 38 to 58 (mean 52) years and weights from 67 to 110 (mean 82) kg. The study was approved by the Göttingen University Human Subjects Review Committee and written informed consent was given by all patients at the time of the pre-operative visit.

No patient gave a history of congestive heart failure or valvular heart disease. Ejection fraction was greater than 40%. None of the patients had either a history or clinical evidence of any metabolic or cerebrovascular disease. All patients were receiving maintenance doses of either calcium-channel blocking drugs (nifidepine 30 mg/day) or beta-adrenoreceptor antagonists (pindolol 15 mg/day) and nitrates (isosorbide 120 mg/day), the last doses of which were given on the morning of the operation.

All patients were premedicated with flunitrazepam 2 mg orally, piritramide 15 mg and promethazine 50 mg intramuscularly one hour before arrival in the anaesthetic room. ECG leads and a five-lead EEG (Lifescan, Neurometrics Inc.) monitored the heart rate, and there was a periodic analysis of the EEG. The following catheters were positioned percutaneously under local anaesthesia: Goodale–Lubin (6-F, USCI) in the radial artery of the nondominant hand to monitor arterial pressure and for blood sampling; a second Goodale–Lubin (6-F, USCI) retrograde into the superior bulb of the right internal jugular vein (Seldinger technique) to monitor pressure, measurement of cerebral blood flow and withdrawal of blood samples; a thermistor-tipped model, (Edwards quadruple thermodilution no. 93A 131-7F) flow-directed into the pulmonary artery via an antecubital vein to measure cardiac output; and a polyethylene one into the superior vena cava for administration of drugs and infusions. The positions of all catheters were confirmed radiologically. Airway carbon dioxide was measured by a Normocap CO_2 Analyzer (Datex CD 102/02 Helsinki). The ECG and all pressures (Statham P 23 IA) were monitored continuously and recorded simultaneously on a 10-channel strip chart recorder (Hellige, Freiburg). The EEG was also monitored continuously and recorded during the study periods using the Lifescan printer.

Rectal temperature was measured and referred to before bypass; during bypass, nasopharyngeal, rectal and venous temperature were monitored, but only the venous blood temperature was used as a reference; this did not differ from the nasopharyngeal temperature by more than 0.5°C at the time of measurement.

Study periods and anaesthesia

Measurements were performed in the awake patient after 30 minutes of rest after catheterisation; 30 minutes after induction of anaesthesia under normothermic conditions; 30 minutes after start of bypass and cross-clamping of the aorta at stable venous and arterial blood temperatures of 26°C.

Anaesthesia was induced with fentanyl 7 μg/kg/minute and midazolam 3 μg/kg/minute. Pancuronium 6–8 mg was administered and after tracheal intubation controlled ventilation with 30% oxygen and 70% air was instituted, using a constant volume ventilator (Engström ER 300). Incremental doses of fentanyl 0.25 mg and midazolam 7.5 mg were given immediately before sternotomy and whenever lightening of anaesthesia was apparent in the EEG.

Cardiopulmonary bypass

The extracorporeal technique consisted of a Polystan heart–lung machine with a membrane oxygenator (Maxima). Forty-micrometre filters (Sartorius, Göttingen) were used in the cardiotomy suction and the arterial line. Priming was with Ringer's lactate 1000 ml, glucose 5% 500 ml, human albumin solution 20% 400 ml, and sodium bicarbonate 100 mmol. Flow was maintained at 1.7–2.2 litres/minute/sq m during bypass. Bretschneider's cardioplegic solution, at 4°C, was infused into the aortic root just after the aorta had been cross-clamped and was removed from the right atrium to prevent uptake into the heart–lung machine. The cooling rate was fast; the temperature of water that entered the heat exchanger was 10–15 °C, but increased to 26°C when venous blood temperature had reached 26°C. Carbon dioxide was added to the oxygenator to maintain a temperature-corrected $P\mathrm{aco}_2$ of approximately 5.3 kPa.

Cerebral blood flow (CBF) measurement and variables

CBF was measured using the argon wash-in technique (coefficient of variation ±5%), described in detail by Tauchert *et al.*[17] This method includes simultaneous blood sampling from the jugular bulb and the radial artery during a period of inhalation of a standard concentration of argon. Argon was administered to the awake patients with a facemask, to the anaesthetised patients through the tracheal tube, and directly into the oxygenator during cardiopulmonary bypass. Saturation periods were 7 minutes before and 10 minutes during bypass.

Before and after each measurement of CBF, blood samples were taken simultaneously from the jugular bulb and the radial artery and analysed for haemoglobin and oxygen saturation and content (CO-Oximeter 282 and Lex-O_2-Con, Instrumentation Lab.), blood gas tensions (standard electrodes, Radiometer), lactate, glucose and pyruvate concentrations (UV methods, standard test combinations, Boehringer Mannheim), and electrolyte concentrations (absorption spectrometry, Perkin Elmer 303). Viscosity of the arterial blood was determined at 37°C and 25°C (Well-Brookfield Cone/Plate Viscosimeter). Cardiac output was measured by thermodilution (cardiac output computer: Fischer BN 7206). Cerebral perfusion pressure (CPP) was calculated as mean arterial pressure (MAP) minus jugular bulb pressure, and cerebral vascular resistance (CVR) as CPP divided by CBF. Cardiac index was calculated by dividing cardiac output by the body surface.

The cerebral metabolic rates (CMR) of oxygen, glucose, lactate and pyruvate were calculated by multiplying the arterial–cerebral venous blood oxygen content and substrate concentration differences, respectively, by the cerebral blood flow. The oxygen–glucose index (OGI) can be calculated from the equation:

Table 1. Haemodynamic variables, viscosity and $Paco_2$ under fentanyl–midazolam anaesthesia alone and in combination with hypothermia of 26°C ($n = 10$ patients). Values expressed as mean (SD).

	I	II	III
HR, per minute	65 (9)	62 (6)	0
MAP, mmHg	92 (7)	71 (10)*	77 (13)
CPP, mmHg	85 (6)	67 (11)*	66 (16)
CI, litres/minute/sq m	3.33 (0.50)	2.43 (0.32)*	1.98 (0.24)**
CVR, $\frac{\text{mmHg}}{\text{ml/minute/100 g}}$	1.67 (0.37)	2.04 (0.38)*	0.95 (0.58)**
CBF, ml/minute/100 g	53 (10)	33 (4)*	81 (27)**
Viscosity, mPa/second	4.26 (0.36)	3.78 (0.20)*	3.19 (0.32)**
$Paco_2$, kPa (temperature-corrected)	5.92 (0.47)	5.54 (0.39)	5.06 (0.42)**

I, awake; II, anaesthesia and normothermia; III, anaesthesia and hypothermic CPB; HR, heart rate; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CVR, cerebral vascular resistance; CI, cardiac index; CBF, cerebral blood flow. $p < 0.05$; * I as compared with II; ** II as compared with III.

Table 2. Cerebral metabolism under fentanyl–midazolam anaesthesia alone and in combination with hypothermia of 26°C ($n = 10$ patients). Values expressed as mean (SD).

	I	II	III
$CMRo_2$, ml/100 g/minute	3.17 (0.54)	2.47 (0.39*)	0.97 (0.27**)
$CMR_{glucose}$, mg/100 g/minute	4.09 (1.41)	3.05 (0.99)	1.41 (0.64**)
$CMR_{lactate}$, µmol/100 g/minute	−1.77 (1.01)	−1.73 (1.08)	−1.97 (2.59)
$CMR_{pyruvate}$, µmol/100 g/minute	−0.33 (0.16)	−0.22 (0.09)	−0.29 (0.26)
OGI, %	119 (54)	116 (23)	98 (57)
LGI, %	4.5 (3.0)	5.5 (4.0)	21.1 (37.9)

I, awake; II, anaesthesia and normothermia before bypass; III, anaesthesia and hypothermic cardiopulmonary bypass. CMR, cerebral metabolic rate; OGI, oxygen–glucose index; LGI, lactate–glucose index. $p < 0.05$; * I as compared with II; ** II as compared with III.

$$OGI = \frac{avDO_2 \cdot 100\%}{6 \cdot avD_{glucose}}$$

where $avDo_2$ and $avD_{glucose}$ represent the arterial–venous differences in oxygen and glucose in mmol/litre. The lactate–glucose index (LGI) can be calculated from the equation:

$$LGI = \frac{avD_{lactate} \cdot 100\%}{2 \cdot avD_{glucose}}$$

Again, substrate concentrations are represented in mmol/litre.

Statistical analyses of the obtained data were performed using the Wilcoxon Matched-pairs Signed rank test; $p < 0.05$ was assigned statistical significance.

Results

Table 1 shows the control values and the haemodynamic responses after induction of anaesthesia and 30 minutes after start of CPB at a venous blood temperature of 26°C. Anaesthesia with fentanyl and midazolam as induction doses followed by infusions led to significant decreases of MAP and CPP of 23% and 21%, respectively, but not below the range of autoregulation. Both pressures were kept unchanged by adjusting the flow of the heart–lung machine during the hypothermic bypass phase. That is why after a significant 27% decrease following induction of anaesthesia, cardiac index decreased by another 19% during bypass (cardiac index means flow in this context). Cerebral vascular resistance first increased by 22% and then decreased by 53%, according to a 38% decrease and a 145% increase in CBF, respectively. Individual values for both indices for each patient are presented in Figure 1.

Viscosity decreased progressively during the study period (by 11% and 16%, respectively), as a result of saline infusions and haemodilution with the priming solution to prevent an increase in viscosity as temperature decreased. It should be emphasised, that during CPB viscosity was measured at 25°C.

When judged as temperature-corrected value, $Paco_2$ was significantly lower during CPB than after the induction of anaesthesia (by 9%) but stayed within the range of normocapnia.

Table 2 shows the control values and the responses of cerebral metabolism to fentanyl–midazolam anaesthesia under normothermic and hypothermic conditions. Anaesthesia itself led to a 22% reduction of $CMRo_2$, which was further reduced by 61% under the influence of nonpulsatile CPB at a venous blood temperature of 26°C. This is equivalent to a Q_{10} value of 2.5. Individual values of all patients for $CMRo_2$ are presented in Figure 1, together with the values for the cerebral venous oxygen saturation, which was markedly elevated during hypothermic bypass because of an increasing CBF. This occurred despite a decreasing $CMRo_2$ under the temperature-corrected acid-base management.

$CMR_{glucose}$ was also reduced progressively (by 25% and 54%, respectively) during the study period, while $CMR_{lactate}$ and $CMR_{pyruvate}$ remained unchanged. The oxygen–glucose index, that indicated the percentage of glucose oxidised, was not significantly reduced in the course of the investigation since the brain's oxygen and glucose uptake decreased proportionally. Lactate–glucose index, which indicates the percentage of glucose anaerobically metabolised, seemed to increase during hypothermic bypass, but this change was not significant because of wide variations of the individual values. Figure 2 shows the changes in neuronal activity on periodic analysis of the EEG. While induction of anaesthesia with fentanyl–midazolam was characterised by

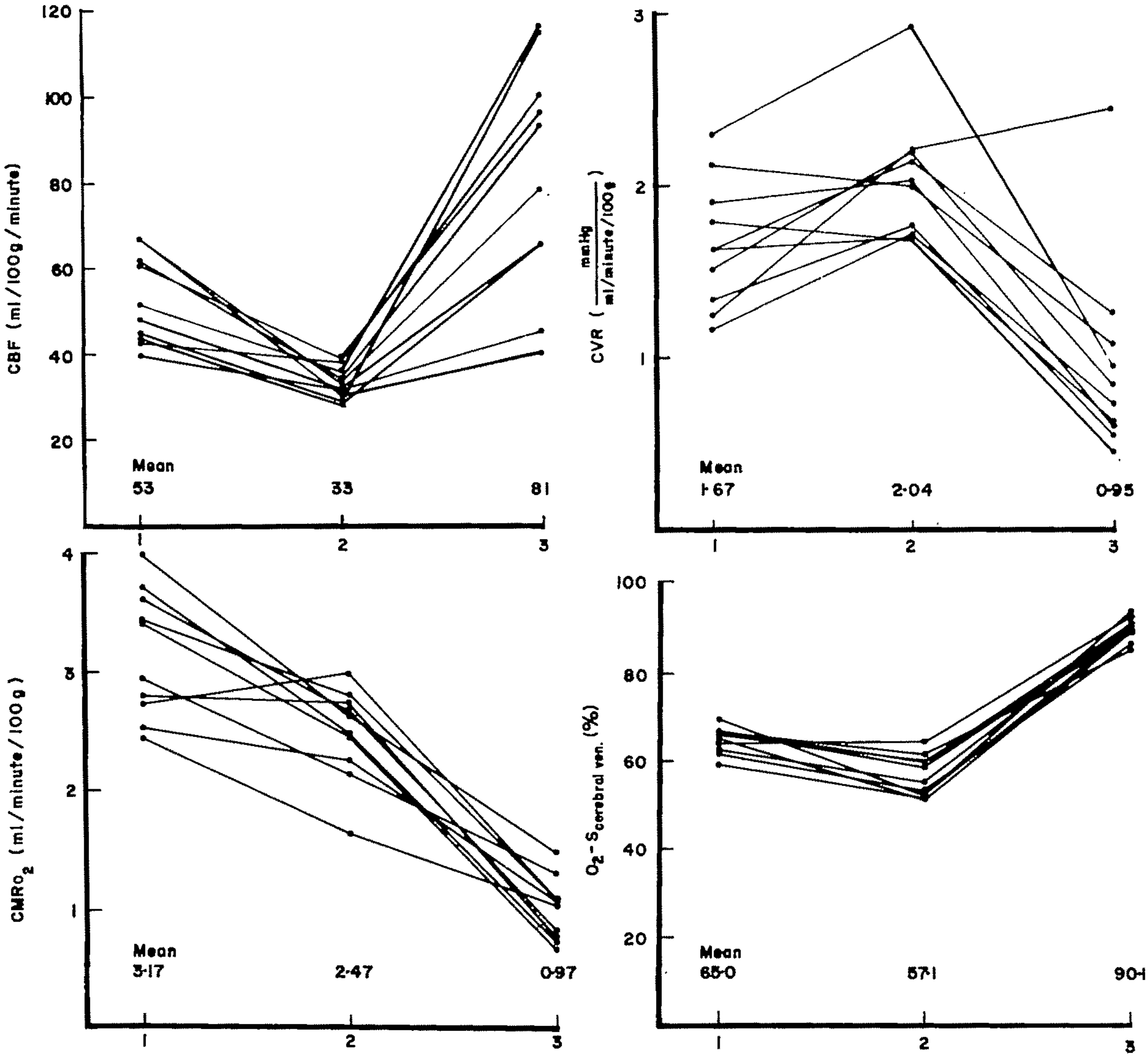

Fig. 1. Individual values for cerebral blood flow (CBF), cerebral vascular resistance (CVR), cerebral metabolic rate of oxygen ($CMRo_2$), and cerebral–venous oxygen saturation ($O_2\text{-}S_{cerebral\ ven.}$) for each patient in the awake state (1), under fentanyl–midazolam anaesthesia during normothermia (2), and during hypothermia of 26°C venous blood temperature (3). Mean values are represented above the abscissa.

a decrease in fast-wave (β) and an increase in high-amplitude, slow-wave (δ) activity, the combination of anaesthesia and hypothermia (26°C) led to an almost complete suppression of EEG activity.

$Paco_2$ and electrolyte concentrations remained within their physiological ranges during the entire study period.

Discussion

The mean control value of 53 ml/100 g/minute for CBF in this study is within the range of normal values obtained with the Kety–Schmidt technique, although at the upper level. This is explained by the fact that our control values were measured in unanaesthetised but heavily premedicated patients with slightly elevated $Paco_2$ values (Table 1). Mean values for oxygen (3.17 ml/100 g/minute), glucose uptake (4.09 mg/100 g/minute) and lactate release (1.77 μmol/100 g/minute) (Table 2) also agree with awake values reported by other investigators,[19] as does the lactate–glucose index (4.5%), while the oxygen–glucose index (119%) is slightly higher than the usually reported normal value of 90–100%. This may be attributed to the relatively lower arterial–venous glucose differences, in relation to the arterial–venous oxygen content differences measured in this study.

Effects of anaesthesia

The results of different laboratories concerning the influence of various anaesthetics on cerebral haemodynamics and metabolism are difficult to compare. This is because cerebral metabolism is much more determined by the depth of anaesthesia than by the anaesthetic agent, while cerebral blood flow is not only dependent on cerebral metabolism (and hence depth of anaesthesia) but also on the anaesthetic agent.[11–15]

Forster *et al.*[20] who studied the effects of midazolam on cerebral haemodynamics in human volunteers, observed a 33% decrease in CBF accompanied by a 39% increase in CVR after a single dose of midazolam 0.15 mg/kg. Nugent *et al.*[13] compared the effects of midazolam and diazepam on canine cerebral metabolism and circulation and found no effects on $CMRo_2$ with midazolam 0.2 mg/kg and diazepam 0.3 mg/kg, while CBF was already reduced by

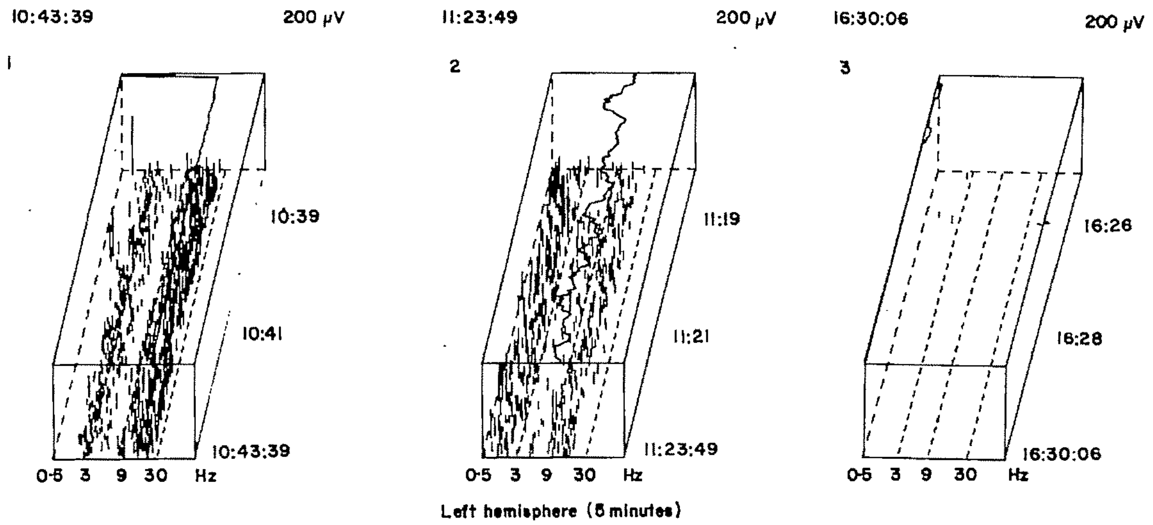

Fig. 2. EEG, as interpreted by a periodic analysis, in the awake but premedicated patient (1), under fentanyl–midazolam anaesthesia during normothermia (2), and during hypothermia of 26°C venous blood temperature (3). Frequency is displayed on the *x* axis. The amplitude of each mapped EEG wave is a vertical 'pole' and is shown at the top of the transparent box, which is 200 µV. Time is displayed on the *z* axis. The displays represent 5 minutes of EEG of the left hemisphere.

45% at these doses. Additional drug administration resulted in dose-related decreases in CMRo$_2$ up to 55% of control with midazolam and to 71% of control with diazepam. Concomitantly, there was a change in the EEG as reflected by a decrease in frequency and an increase in amplitude. The largest decreases in CBF were 49% with diazepam and 69% with midazolam. As their dogs were maintained on nitrous oxide and halothane, the results of Nugent *et al.*[13] might be influenced by these two anaesthetic agents, which could explain the striking differences between their data and those of Carlsson *et al.*[21] This study reported that in rats diazepam in sedative and anaesthetic doses (0.75 and 7.5 mg/kg) did not change CMRo$_2$ in the absence of nitrous oxide, while the addition of 70% nitrous oxide decreased CMRo$_2$ to about 60% of control.

The responses of cerebral haemodynamics and metabolism to certain anaesthetic drugs may also be altered by the age of the studied species. Baughman *et al.*[22] observed a decrease in CBF and CMRo$_2$ by 51% and 38%, respectively, produced by 5.75 mg/kg of midazolam in the presence of 70% N$_2$O in young rats, but a 62% decrease in CBF and a 59% decrease in CMRo$_2$ in old rats. Fentanyl (200 µg/kg), however, decreased CBF by 49% and CMRo$_2$ by 39% in young rats, whereas in old rats the same fentanyl dose decreased CBF by 37% and CMRo$_2$ by 34%. This indicates that ageing attenuates the cerebrovascular and cerebral metabolic depression produced by fentanyl, but potentiates the same effects produced by midazolam.

Patients of the present study ranged in age from 38 to 58 years; thus our results represent an average of both younger and older patients.

The depressant effects of the fentanyl–midazolam combination on CBF and cerebral metabolism are similar to those previously reported,[20–22] although the degree of depression is lower, which might be related to the absence of nitrous oxide and to the depth of anaesthesia. The dosage of fentanyl and midazolam chosen in the present study provided haemodynamic stability combined with adequate anaesthesia, as shown by an increase in high-amplitude, slow-wave activity in the EEG (Fig. 2). Hence, it was not necessary to deepen anaesthesia until burst suppression occurred, which certainly would have aggravated the cerebral depressant effects of both drugs. The significant decreases in MAP and CPP by 23% and 21%, respectively, cannot account for the decrease in CBF, since they remained in the physiological range for cerebral blood flow autoregulation. The decrease in viscosity (Table 1) would have led to an increase in CBF, while the *P*aco$_2$ value did not change significantly, and thus was not responsible for the decrease in CBF. Our results are consistent with those of Vernhiet *et al.*[12] who, studying the effects of a diazepam–fentanyl/N$_2$O mixture on cerebral blood flow and oxygen consumption in man, found a 34% decrease both in CBF and CMRo$_2$. They concluded, that the coupling of flow and metabolism was maintained, which was confirmed by the constancy of jugular venous oxygen tension. This is in contrast to our study, where the combination of midazolam and fentanyl produced a greater decrease in CBF than in CMRo$_2$, as shown by the slight decrease in jugular venous oxygen saturation (Fig. 1). CMRo$_2$ and CMR$_{\text{glucose}}$, on the other hand, changed to the same extent (Table 2); thus OGI as an index of aerobic metabolism remained unchanged as did the LGI as an index of anaerobic metabolism.

Effects of hypothermic cardiopulmonary bypass

Hypothermia led to an isoelectric burst/suppression EEG pattern (Fig. 2) with predominantly isoelectric periods. Neither anaesthesia nor hypothermia of 26°C alone are able to produce such a deep suppression of neuronal activity. This is confirmed by Quasha *et al.*[23] for the combination of barbiturates and hypothermia in man. Steen *et al.*[24] reported that in the unanaesthetised dog EEG became isoelectric below temperatures of 18°C, while at 28°C the EEG was normally active but could be suppressed to isoelectricity by thiopentone. This led to a significant reduction of CMRo$_2$, whereas at 18°C the addition of the drug had no further effect on $CMRo_2$, when the EEG manifested no activity already without thiopentone. Thus the difference between barbiturates and hypothermia is that barbiturates decrease cerebral metabolism only in the presence of EEG activity, while hypothermia reduces $CMRo_2$ by affecting rate-limiting reactions regardless of the functional state. Whether in the absence of electrophysiologic function, there is a log-linear relationship between temperature and $CMRo_2$ (following an Arrhenius curve), as suggested by Steen *et al.*[24] and Astrup *et al.*[25] or simply a rectilinear one, as suggested by Hägerdal *et al.*[26] cannot be decided from the present study.

We found a 61% decrease in $CMRo_2$ at 26°C venous blood temperature (Table 2), which is equivalent to a Q_{10} value of 2.5. This is in close agreement with Q_{10} values derived from animal studies[24,25,27] while Woodcock *et al.*[28] saw a markedly stronger depression of $CMRo_2$ by 73% at comparable temperatures in patients in whom EEG activity was present, and by 89% in patients in whom EEG was suppressed by thiopentone. Murkin,[5] who belonged to the same group, found a 75% decrease in $CMRo_2$ at a mean nasopharyngeal temperature of 26.6°C. These conflicting results are not easy to explain, but may be attributable to different anaesthetic and cardiopulmonary bypass techniques.

The 61% decrease in $CMRo_2$ in the present investigation was accompanied by a nearly equal reduction in $CMR_{glucose}$, by 54% at 26°C venous blood temperature. This meant that OGI did not change significantly, which implied that aerobic metabolism of glucose is the predominant method for cerebral energy production even under the conditions of hypothermic cardiopulmonary bypass. This is confirmed by data obtained in dogs by Astrup *et al.*[25] and Michenfelder and Theye.[27] The statistically insignificant increase in LGI associated with wide variations of the $CMR_{lactate}$ values, may be attributed to the fact that the lactate ion poorly penetrates the blood–brain barrier. Thus, cerebral venous blood lactate measurement may inadequately reflect cerebral metabolism[27] especially when arterial–venous differences are very small.

In spite of the hypothermia-induced depression of cerebral metabolism, cerebral blood flow was found to be greatly elevated, and led to an uncoupling of flow and metabolism, i.e. a luxury perfusion of the brain, characterised by high venous oxygen saturation values (Fig. 1). This cannot be caused by changes in mean arterial or cerebral perfusion pressure (Table 1), nor by an increase in systemic flow (pump volume). Anaesthesia itself cannot be responsible for this hyperperfusion either, since fentanyl–midazolam anaesthesia decreases CBF under normothermic conditions. The small decrease in viscosity, only partly contributes to a luxury perfusion of this degree. The main factor is probably the addition of CO_2 to the oxygenator to maintain a temperature-corrected $P\text{aco}_2$ of 5.3 kPa, which means a $P\text{aco}_2$ of 8.7 kPa if temperature-uncorrected. Henriksen[4] found an increase in CBF from a prebypass level of 29 ml/100 g/minute to a value of 49 ml/100 g/minute at 27°C in a group of patients in whom 3–5% CO_2 was added to the oxygenator. This was to maintain temperature-corrected $P\text{aco}_2$ values of about 5–5.2 kPa, while, when no CO_2 was added, hyperperfusion during bypass was largely avoided. Nevertheless, although Henriksen[4] recognised CO_2 tension to have an important influence on CBF, he considered hyperperfusion not only to be related to the effect of CO_2 but also to progressive micro-embolisation during bypass.

Govier *et al.*[7] found a 55% decrease in CBF, with nasopharyngeal temperature and $P\text{aco}_2$ the only two significant factors that influenced CBF during bypass. Andersen[3] on the other hand found that nonpulsatile flow affects the metabolic flow regulation in the brain by interfering with the myogenic contractility of cerebral arterioles, in contrast to pulsatile flow at normothermia.

Two further studies have been published, concerning the relationship between $P\text{aco}_2$ and CBF during nonpulsatile cardiopulmonary bypass at various temperatures.[5,6] These point out that variations in the acid-base management account for most of the differences in CBF values reported by several groups. Murkin[5] compared a temperature-corrected group ($P\text{aco}_2$ 5.3 kPa) with a nontemperature-corrected group of patients ($P\text{aco}_2$ temperature-corrected 3.6 kPa) and found a correlation between CBF and CPP in the temperature-corrected group, while in the nontemperature-corrected group CBF correlated only with $CMRo_2$. Consideration of our results and those of others makes it advisable to practice a nontemperature-corrected acid-base management, which means not to add CO_2 to the oxygenator irrespective of the anaesthetic technique, since during hypothermia a nontemperature-corrected $P\text{aco}_2$ value of 5.3 kPa seems to preserve cerebral autoregulation and maintains a more physiologic relationship between CBF and metabolism.

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CASE REPORT

Epidural anaesthesia and spinal arachnoiditis

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Summary

Six patients were referred to our hospital with spinal arachnoiditis after epidural anaesthesia performed one month to 3 years before the onset of symptoms. None had had previous lumbar surgery or trauma, intraspinal haemorrhage, infections or other known causative factors of arachnoiditis. All the patients were free of neurological symptoms before epidural anaesthesia and only two had transient distress in the period immediately following the procedure. The clinical signs and symptoms of spinal arachnoiditis were severe and in every case the diagnosis was confirmed by myelography. Three patients were confined to a wheelchair after 3 years of follow-up. To our knowledge, the anaesthetic procedures were performed according to standard methods. Arachnoiditis seems to be due to the epidural injection of foreign substances, and may be related to anaesthetic–vasoconstrictor solution or contaminants.

Key words

Anaesthesia, regional; epidural.
Complications; arachnoiditis.

Transient and, exceptionally, permanent neurological complications due to haematoma[1-5] or hypotension[6,7] have been reported after epidural anaesthesia. Nevertheless, this is a widely employed, easily performed procedure which is considered generally to be safe.

Spinal arachnoiditis may occur as a delayed complication of some diagnostic and therapeutic procedures which require the introduction of foreign substances into the subarachnoid space. This is the case for myelography,[8-10] subarachnoid administration of sulpha drugs, penicillin and corticosteroids,[11] antitetanus serum,[12] and subarachnoid anaesthesia.[13-16]

Up to 1983 we had observed four cases (patients referred to as cases 1–4 in the present paper) of severe and diffuse arachnoiditis which followed epidural anaesthesia.[17] Only four similar cases had been reported at that time;[18-20] inadvertent injection of the anaesthetic solution into the subarachnoid space was implicated in all four, although detergents may have contributed in two. We wish to present our overall experience of spinal arachnoiditis following epidural anaesthesia, which now includes six patients.

Case histories

Six patients (four male) aged 18–44 years, referred by different hospitals, developed irreversible neurological deficits after epidural anaesthesia performed 1 month to 3 years earlier. Five patients were admitted to the Istituto Neurologico 'C. Besta' of Milan, and one was hospitalised elsewhere. Three patients had received epidural anaesthesia for plating of a lower limb fracture, two for inguinal herniorrhaphy and one for long saphenous vein stripping. All patients were completely free of neurological deficit before the block and none had had previous back surgery, trauma, haemorrhage, meningitis or other known causative factors of arachnoiditis.

Case 1

A 26-year-old man underwent epidural anaesthesia for inguinal hernia surgery. The anaesthetic procedure was performed in the second lumbar interspace employing bupivacaine hydrochloride 0.5% 18 ml (90 mg) and adrenaline 1:200 000 without any complication. He complained of a sharp low back pain one month later which subsided over the next 4 weeks. Soon afterwards, he developed progressive asymmetrical lower limb weakness. On admission to our Institute one year later, he showed asymmetrical wasting and weakness of the legs, increased lower limb tendon reflexes and hypoaesthesia of the medial

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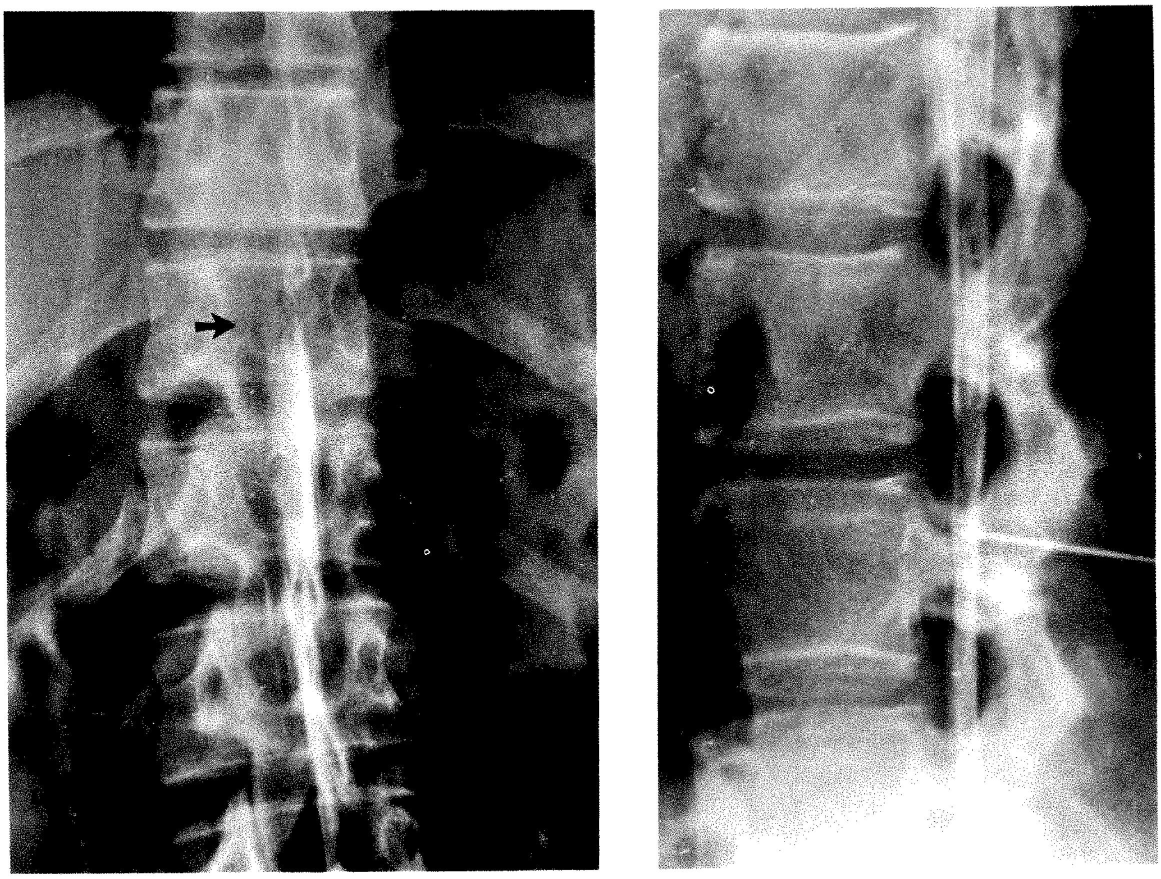

Fig. 1 Lumbar myelography (Iopamiro 300, 2 ml). *Left:* anteroposterior; *right:* lateral projection. Adhesive arachnoiditis with complete block of contrast medium progression at the T_{10}–T_{11} level (arrow).

surface of the right leg. Myelography revealed middle and low thoracic arachnoiditis with spinal cord atrophy. He was confined to a wheelchair for most of the time when last seen 4 years later.

Case 2

A 21-year-old female had two successive operations under epidural anaesthesia within 4 months for plate insertion and removal because of a right tibial fracture. The first anaesthetic was performed with bupivacaine hydrochloride 0.5% 10 ml (50 mg) with adrenaline 1:200 000 and mepivacaine hydrochloride 2% 9 ml (180 mg). The second anaesthetic procedure was performed with bupivacaine hydrochloride 0.5% 17 ml (85 mg) and adrenaline 1:200 000. The patient remembers that she complained of low back pain in the first few days after the second block, although this was not mentioned in the clinical record. Between 3 and 4 months after the second block she noted difficulty in walking and urinary urgency with episodic incontinence. Six months later, a suboccipital myelogram performed in our Institute after unsuccessful lumbar puncture, showed arachnoiditis from C_7–T_9 with complete block at the lower level. Neurological examination showed a spastic hyperreflexic paraparesis, bilateral Babinski sign, hypoaesthesia from the umbilical segment downward and urinary incontinence. The clinical picture was similar 5 years later, and she was unable to walk without a crutch.

Case 3

This male patient underwent several operations within one year, three of them under epidural anaesthesia for surgical procedures to a fractured lower leg. At the time of injury, he was 16 years of age. The first epidural block was performed with mepivacaine hydrochloride 2% 19 ml (380 mg), the second with bupivacaine hydrochloride and mepivacaine hydrochloride (doses not specified) and the third with bupivacaine hydrochloride 0.5% 20 ml (100 mg) and mepivacaine hydrochloride 2% 2 ml (40 mg) supplemented with intravenous ketamine hydrochloride 50 mg. He complained of a painful paraesthesia during the third block, and 4 hours later of lumbar pain, which remitted within one hour after administration of intramuscular aminopyrine 500 mg. Six days later, he complained of headache (type and duration not specified).

One month after the last anaesthetic, he showed a progressive hyperreflexic spastic paraparesis, with urinary incontinence and hypoaesthesia to all modalities up to the nipple level. He developed intracranial hypertension with associated papilloedema 3 months later. Computerised tomography showed hydrocephalus; myelography revealed a severe and diffuse spinal arachnoiditis (Fig. 1). A ventriculoperitoneal shunt performed in our Institute produced an improvement in his clinical condition which was maintained for the next 18 months. Subsequently, he complained of a progressive deterioration, with lower limb weakness, hypoaesthesia and weakness of the left arm and face. After a year with no change in symptoms and signs,

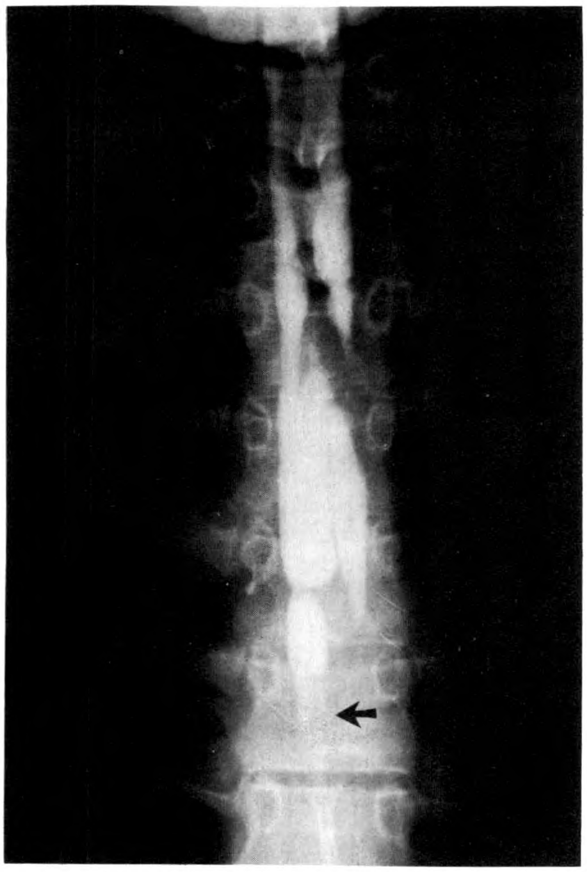

Fig. 2 Suboccipital water-soluble contrast medium myelography: arachnoiditis in the dorsal tract with complete block at the T_7 level (arrow).

dysarthria, dysphonia and dysphagia appeared, together with inability to walk. Magnetic resonance imaging showed a syringomyelic cavity that extended upward into the medulla, with multiple cavitations of the pons and midbrain, connected to larger cavities in the right cerebellar hemisphere and right temporal lobe.[21]

Case 4

An 18-year-old man was submitted to epidural anaesthesia for plating of an exposed fracture of the right femur. The block was performed in the third lumbar interspace with bupivacaine hydrochloride 0.5% 90 mg (18 ml) and adrenaline 1:200 000. The immediate postoperative course was uneventful, but he began to complain of bladder dysfunction, lower limb sensory impairment and stiffness 10 months later. Neurological examination 4 months later, on admission to our Institute, showed spastic hyperreflexic paraparesis and sensory impairment with the upper limit at the lower ribs. He could not walk or stand unaided. Suboccipital myelography, performed after unsuccessful lumbar puncture, demonstrated diffuse arachnoiditis from T_2 with complete block at T_7 (Fig. 2). A brain CT scan was normal. He was still confined to a wheelchair 4 years later.

Case 5

A 40-year-old man underwent surgical repair of an inguinal hernia under epidural anaesthesia. No anaesthetic chart was completed, but at that time, the anaesthetic team working in the hospital routinely performed epidural anaesthesia in the second lumbar interspace with bupivacaine hydrochloride (probably 0.5%, 12.5–25 ml) with or without adrenaline 1:200 000. No postoperative complication was reported either by the patient or in the clinical record. He was admitted to our Institute 4 years after surgery, with a 12-month history of progressive lower limb weakness, distressing lumbar and left sciatic pain, bladder spasms and impotence. Neurological examination showed severe spastic hyperreflexic paraparesis, left Lasègue sign and loss of sensation below the inguinal level. Myelography showed thoracolumbar arachnoiditis. Six years after surgery we contacted him by telephone and found that he was in a department for pain treatment; there had been no change in neurological symptoms.

Case 6

A 34-year-old woman was treated surgically for long saphenous vein stripping under epidural anaesthesia. One year later, she began to experience fatigue in walking, difficulty in climbing stairs, low back pain with bilateral sciatic radiation and she felt her legs becoming 'smaller'. A myelogram demonstrated thoracolumbar arachnoiditis. Neurological examination showed a spastic hyperreflexic paraparesis, bilateral Babinski sign and moderate asymmetrical lower limb muscle wasting, with no sensory or sphincter impairment when seen by us 18 months after surgery. We have been unable to obtain information about the anaesthetic technique, and have failed to trace the patient for follow-up.

Further details

We have spoken directly to our colleagues in the other anaesthetic services involved. We have seen the anaesthetic charts of patients 1, 2 and 4 and the expert medical legal report concerning patient 3; we obtained reliable information about patient 5. It would seem that a single disposable needle was introduced into the epidural space in all these five cases (the precise type of needle is never specified in anaesthetic charts although 16–18 Tuohy needles were used routinely). A loss-of-resistance technique with saline was used. After a test dose, analgesia was obtained by single shot epidural, without catheter. Multiple dose vials of local anaesthetic were employed. A glass syringe was used in all cases for detection of the epidural space, but the local anaesthetic solution was injected with a single disposable plastic syringe, at least in cases 1 and 4. Glass syringes were washed with unknown detergents and sterilised by heat in cases 1 and 4; we have no definite information about washing and sterilisation procedures in the remaining cases. Hypotension or other intra-operative complications were not recorded in any of the procedures. We can infer from clinical records and direct information from the patients that the epidural block lasted 3 to 5 hours in all cases except case 2; she remembered that her second block lasted about 8 hours. Complete and rapid recovery occurred in the two patients in whom paraesthesia or lumbar pain developed during or soon after anaesthesia.

No patient had fever, local spine tenderness or signs of nonneurological illness when first seen in our Institute. Five patients had normal cerebrospinal fluid (CSF); the concentration of protein was elevated slightly in case 3 (0.62 g/litre, normal value 0.20–0.45 g/litre). Thoracolumbar arachnoiditis was found at myelography in every patient (Figs 1–2).

All patients showed a slowly progressive deterioration in symptoms and signs during the follow-up period (1 to 5 years). Three subjects were confined to a wheelchair within 4 years of the onset of illness.

Discussion

All our patients presented with neurological symptoms caused by a chronic arachnoiditis; this diagnosis was confirmed by myelography. The possibility that epidural anaesthesia, the only common point in the history of all our patients, was responsible for arachnoiditis is suggested by the absence of other possible causes; the chronological relationship between onset of illness and the anaesthetic procedure (this period was short in all patients except number 5, although even the interval in this case does not exceed those reported previously);[11,22] and the previous descriptions of similar cases in the literature.[18–20]

The lack of history of meningitis and CSF abnormalities rules out infection as the cause of arachnoiditis, even though early CSF examinations were not performed and two patients were known to have had transient headache and lumbar pain after epidural anaesthesia. Other authors[13,16,23] have suggested that contamination of anaesthetic instruments may induce an arachnoiditic reaction. Detergents were demonstrated experimentally to induce arachnoiditis in animals[14] and to cause chemical arachnoiditis after spinal anaesthesia.[16,19,23] It is possible that they might produce the same reaction after introduction into the epidural space.[19] In all of our cases, a glass syringe was used for identification of the epidural space, and contamination by detergents must be considered. In at least two cases, a disposable plastic syringe was employed for injection of local anaesthetic solution after identification of the epidural space. Therefore, detergents would have been present only in very small quantities if at all. Nevertheless, we can neither exclude nor confirm the possibility that detergents were responsible for the subsequent neurological changes in our patients. Detergents should never be used for anaesthetic tray preparation and single disposable syringes and needles should always be used for epidural anaesthesia.[19]

Another possible explanation is that the anaesthetic–vasoconstrictor solution itself brought about the meningeal reaction. Anaesthetics can induce arachnoiditis if injected subdurally.[14,15] Injection of local anaesthetic solution into the subarachnoid space during epidural analgesia is uncommon. None of our patients displayed the features of total spinal anaesthesia. However the anaesthetic solution might have reached the subarachnoid space not only through inadvertent and direct introduction in small quantities during the anaesthetic procedure[18–20] but also through direct diffusion across the dura or centripetal spread through the dural root cuffs.[24] In both live and dead animals, anaesthetic drugs have been found in CSF after epidural injection.[25,26]

Multiple dose vials of local anaesthetic solution contain parabens (methyl and propyl-paraben) as preservatives. These compounds are constituents of some dermatological preparations, and are known to cause severe and intractable contact dermatitis;[27] in the United States and Canada, it has been recommended for many years that they should not be employed in solutions used for caudal or epidural anaesthesia.[28]

Case 3 is particularly interesting because of the considerable progression of the disease. He developed a myelographically diagnosed spinal arachnoiditis and hydrocephalus ascribable to intracranial subarachnoid obstruction. In the next 30 months he presented a rare complication of arachnoiditis, namely cervical syringomyelia,[29,30] and developed a cranial extension of the cavity upward to the midbrain with cerebellar and cerebral cavitations.

Previous reviews[31–33] report an absence, or low incidence, of neurological complications following epidural anaesthesia (0.1% transitory paresis and 0.02% permanent sequelae in 32 718 examined cases).[34] However, it should be considered that spinal arachnoiditis may have its onset months or even years after epidural anaesthesia and therefore easily escapes routine anaesthetic follow-up; in addition, neurologists may fail to consider the patient's anaesthetic history when treating a patient with arachnoiditis. The true incidence of this complication may have been underestimated.

Acknowledgment

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* Ref. 17: there are obvious mistakes in the indication of dosages of anaesthetic and vasoconstrictor. Correct dosages employed are reported in the present paper.

Anaesthesia, 1989, Volume 44, pages 322–323

CASE REPORT

Termination of paroxysmal supraventricular tachycardia by intravenous adenosine in a child

A. E. CHOW AND C. NOBLE-JAMIESON

Summary

A fit 6-year-old child developed paroxysmal supraventricular tachycardia at the end of an operation for adenotonsillectomy. Sinus rhythm was rapidly restored with intravenous adenosine.

Key words

Heart; arrhythmia, ventricular tachycardia.

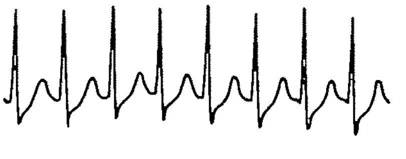
Sinus tachycardia in response to sympathetic stimulation at light levels of anaesthesia occurs frequently during surgery, particularly immediately after induction and intubation of the trachea. The occurrence of paroxysmal supraventricular tachycardia (PSVT), however, is an unusual event and may occur without evidence of any pre-existing cardiac abnormality. We report here an episode of PSVT which took place at the conclusion of surgery before extubation.

Case history

A 6-year-old girl who weighed 21 kg was admitted for routine tonsillectomy and adenoidectomy. Pre-operative assessment revealed no significant medical history or physical findings. She was premedicated with trimeprazine syrup 50 mg and atropine 0.4 mg, given by mouth 1.5 hours before operation. The ECG was monitored continuously throughout the operation. Induction was with thiopentone 75 mg and suxamethonium 25 mg, and the trachea was intubated with a 5.5-mm tracheal tube, and when spontaneous ventilation had returned, anaesthesia was maintained with halothane 1.5–2% in 30% oxygen and nitrous oxide, through an Ayre's T-piece. Papaveretum 3 mg was given intramuscularly for analgesia after the operation, just before surgery started.

The operation was uneventful but towards the end of the procedure, when anaesthesia was being reduced, a sudden increase in pulse rate was noted and the ECG showed a supraventricular tachycardia of about 250 beats/minute. All anaesthetic agents were stopped and the patient's lungs were ventilated with 100% oxygen. Left carotid massage was carried out and produced a transient reduction in heart rate to 150 beats/minute, but the rate returned to 250 beats/minute within 20 seconds. There was no response to gentle ocular pressure.

A 12-lead ECG was performed at this stage; this confirmed the diagnosis of supraventricular tachycardia (Fig. 1), and the patient began to show signs of recovery from the anaesthetic. Adenosine 1.0 mg (0.05 mg/kg) was administered intravenously and within 20 seconds the PSVT was converted to sinus tachycardia with a rate of 150 beats/minute. The patient had by now recovered consciousness and throughout the whole episode there had been no cyanosis, and perfusion was deemed to be normal. She was transferred to the Intensive Therapy Unit and overnight cardiac monitoring revealed no further episodes of PSVT. Her subsequent recovery was uneventful.



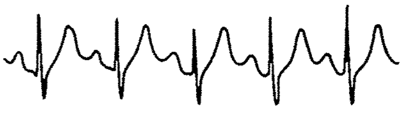


Fig. 1. Electrocardiogram trace showing paroxysmal supraventricular tachycardia before and after intravenous adenosine.

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Discussion

Anaesthetic considerations in patients deemed to be particularly susceptible to PSVT were reviewed in this journal.[1] Avoidance of agents which may predispose to PSVT was recommended and the use of verapamil and propranolol in the management of three cases of established PSVT was described.

Verapamil has been advocated as the drug of first choice in children although it may cause hypotension, persistent bradycardia and even death.[2,3] Cardioversion, while likely to be effective, may cause myocardial necrosis particularly if repeated attempts to restore sinus rhythm are necessary.

The anti-arrhythmic properties of adenine compounds were first noted experimentally more than 50 years ago by Drury and Szent-Gyorgi,[4] and in 1955 Somlo[5] described the use of adenosine triphosphate (ATP) in PSVT. However, the use of ATP is frequently associated with transient side effects such as malaise, hyperpyrexia, flushing, headache and vomiting, with one case of bronchial asthma and another of convulsions also reported. Sinus arrest, sinus bradycardia and varying degrees of atrioventricular block, again of a transient nature, are also described.[6]

Adenosine, the endogenous purine nucleoside formed as an *in vivo* degradation product of ATP, appears to be free of these side effects.[7] Moreover it seems to be safe in severely ill children for the acute termination of PSVT, although, because of its transient action, is of no value in the long-term management.

The adenosine used in this patient was provided by the Department of Paediatric Cardiology at the Brompton Hospital, London, as part of a multicentre study to evaluate its use in PSVT in children. Anaesthetists who might encounter PSVT in children undergoing surgery should be aware of the potential risks of intravenous verapamil and should consider the use of adenosine, if the results of the multicentre trial are favourable.

Acknowledgments

We thank Drs J. Till, E. Shinebourne and M. Rigby of the Department of Paediatric Cardiology, Brompton Hospital, London, for permission to report this case from their multicentre trial of the use of adenosine in children. We are grateful to Mr I. Lord, Consultant ENT Surgeon, for permission to publish details of this case.

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Anaesthesia, 1989, Volume 44, pages 324–325

CASE REPORT

Respiratory arrest after a caudal injection of bupivacaine

A. B. LUMB AND F. CARLI

Summary

A 3.5-year-old child with Cornelia de Lange syndrome presenting for orchidopexy and herniotomy received general anaesthesia which was supplemented by a caudal injection of bupivacaine. Shortly after this he had a respiratory arrest with fixed dilated pupils. No cardiovascular system instability was observed. Approximately one hour later the child made a rapid and complete recovery. The possible causes of these events are discussed with particular reference to the potential effects of caudal injections on intracranial pressure.

Key words

Anaesthesia; caudal.
Complications; respiratory arrest.

Caudal anaesthesia is a technique used widely for both intra- and postoperative analgesia, and is particularly useful in children who have lower abdominal or anogenital surgery. Complications such as accidental subarachnoid and intravascular injections are well documented.[1,2] We report a case of a child who, after a caudal injection, had a respiratory arrest and developed severe neurological complications.

Case history

A 3.5-year-old boy who weighed 10.8 kg presented for elective surgical correction of a left undescended testicle and bilateral inguinal herniae. He had been diagnosed as having Cornelia de Lange syndrome at birth, but his mental and physical development was less impaired than had been originally predicted from his condition. He was generally fit and well apart from frequent mild upper respiratory tract infections.

He was recovering, on admission, from a further respiratory infection, for which he had just completed a course of cotrimoxazole. He had no fever or other clinical signs of chest infection, and his chest X ray was normal.

He was premedicated with papaveretum 2.5 mg and hyoscine 0.05 mg intramuscularly 90 minutes before operation. General anaesthesia was induced with halothane in a mixture of nitrous oxide in oxygen and spontaneous ventilation was maintained throughout. Intravenous access was established. A standard aseptic technique was used and a 23-G needle was inserted into the caudal canal and 8 ml 0.25% bupivacaine injected. No blood or cerebrospinal fluid was aspirated. The patient's pulse rate and oxygen saturation were monitored throughout induction of anaesthesia. He was then moved into theatre and monitoring that included electrocardiogram, noninvasive blood pressure and pulse oximetry established. The child's spontaneous breathing ceased at this time, approximately 2 minutes after the caudal injection. His pupils were widely dilated with no response to light.

Anaesthesia was stopped and surgery abandoned. Intermittent positive pressure ventilation of the lungs was started with 100% oxygen through a mask, followed by tracheal intubation which did not elicit a response from the child. His heart rate at this time was 115/minute, systolic blood pressure 80 mmHg and oxygen saturation 100%. An intravenous infusion of compound sodium lactate solution was started at 40 ml/hour. Fifteen minutes later he remained unchanged with widely dilated pupils, generalised atony, and stable cardiorespiratory parameters. He was then transferred to the intensive therapy unit for further artificial ventilation.

Investigations carried out at this stage revealed normal arterial blood gases, electrolytes, and glucose; a haemoglobin of 10.6 g/dl and a white cell count of 32 × 10^9/litre (63% lymphocytes). His clinical condition remained unchanged.

One hour later his pupils became smaller, he began moving all four limbs, and spontaneous ventilation returned. He removed the tracheal tube himself within 10 minutes and apart from being a little drowsy, he was back

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to normal with no residual neurological sequelae. There was no evidence of any remaining motor or sensory block, but assessment of this was difficult because the child was distressed by his new surroundings.

Postoperatively he developed an upper respiratory tract infection which necessitated a further 2 days' stay in hospital, and during this time no other cause for his leucocytosis was found. He was generally well on subsequent follow-up.

Discussion

This child suffered a rapid, and temporary, neurological deterioration after a caudal injection during an otherwise uncomplicated general anaesthetic. The most severe manifestations were apnoea and bilateral fixed dilated pupils, which both indicate that a significant brainstem or midbrain insult occurred.[3] His cardiovascular system remained surprisingly stable despite this.

The child presented with the congenital abnormality of Cornelia de Lange syndrome, features of which include abnormal muscle tone and mental retardation.[4] There were no specific abnormalities of the central nervous system which may have been expected to complicate either regional or general anaesthesia. The one reference in the literature to the anaesthetic management of the syndrome highlighted potential problems with seizures, cardiac abnormalities, or difficult intubation.[5]

The speed of onset of the neurological signs observed in this child might indicate that accidental intravascular injection had occurred, possibly through intraosseous placement of the needle. However, our dose of 20 mg of bupivacaine was within the accepted 'safe' dose[1] and signs of systemic bupivacaine toxicity such as cardiovascular instability and seizures were not observed.[6]

Accidental subarachnoid injection is another complication of caudal extradural blockade. However, in this case, the sequence of events was too sudden and there were no cardiovascular disturbances which would have been expected after such an extensive block.[6] We are not aware of a case of accidental sub-dural injection after a caudal block. The clinical signs are similar to subarachnoid injection and take even longer to develop when this complication follows lumbar extradural injections.[2,7] In addition, a gradual segmental recovery which would have been expected after either a sub-dural or subarachnoid injection did not occur.

The occurrence of respiratory arrest might also result from a sudden increase in intracranial pressure (ICP), which can be associated with compression of the third cranial nerve on the tentorium and results in pupillary dilatation.[3] A significant increase in ICP has been shown to occur after a lumbar extradural injection of only 10 ml of local anaesthetic solution in adults. Furthermore, this increase is particularly marked if the ICP is raised before injection.[8] Semple and Bisset have reported a transient loss of consciousness after caudal injections, which they ascribed to a rapid rate of injection which increases the ICP.[9] Similarly, apnoea and loss of consciousness that lasted about 5 minutes has been reported by Abouleish following the caudal injection of 22 ml of local anaesthetic solution in adults with intracranial space-occupying lesions.[10]

Our child had no evidence of raised ICP before operation; the duration and intensity of the signs was greater than in the above reports and the reasons for this remain unclear. It is however possible that the caudal injection raised ICP to such an extent that prolonged respiratory arrest occurred.

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Anaesthesia, 1989, Volume 44, pages 326–327

CASE REPORT

Pulse oximetry in methaemoglobinaemia

Failure to detect low oxygen saturation

H. U. RIEDER, F. J. FREI, A. M. ZBINDEN AND D. A. THOMSON

Summary

The results of pulse oximetry saturation in a patient with a high level of methaemoglobinaemia, who subsequently underwent intravenous methylene blue treatment, are presented. The reasons for the erroneously low values after treatment are explained. Pulse oximeters currently available are not helpful in patients treated with methylene blue and should be used with caution in patients who present with cyanosis of unknown origin.

Key words

Equipment; pulse oximeter.
Complications; methaemoglobinaemia.

Pulse oximetry measurement of oxygen saturation in 'arterial' blood has evolved into a very valuable monitoring tool. However, the accuracy of this method may be affected by several factors: low saturation in the range of less then 50% may result in overestimation,[1] several therapeutic and diagnostic dyes[2–4] as well as methaemoglobinaemia[5,6] may also disturb the measurement. We report the results of pulse oximetry analysis in a 20-year-old woman with a high level of methaemoglobinaemia (64%), who subsequently was treated with methylene blue.

Case history

A 20-year-old Italian woman, weight 72 kg, height 170 cm, was admitted to the emergency ward with a 19-hour history of brownish-blue skin colour, dyspnoea and vomiting. She had been found collapsed and unresponsive shortly before admission.

She had cyanosis and hyperventilation at a rate of 34 breaths/minute in the emergency room; hyperventilation slowed to a Cheyne–Stokes breathing pattern. Arterial blood pressure remained at values of 120/50 mmHg with sinus tachycardia of 110 beats/minute. Body temperature and auscultation of heart and lungs were normal. Neurological assessment revealed a patient unresponsive to pain with both pupils sluggishly reacting and slightly mydriatic, hyper-reflexia of the biceps and quadriceps muscles, clonus of the right forearm and both feet, and the Babinsky test could not be elicited.

The patient's trachea was intubated after intravenous administration of diazepam, thiopentone and suxamethonium. Anaesthesia was maintained with thiopentone, fentanyl and pancuronium. Blood pressure remained at 120/80 mmHg and pulse rate at 110 beats/minute.

Insertion of an arterial line revealed brownish-blue coloured blood. Arterial blood gases during intermittent positive pressure ventilation (IPPV) with 100% oxygen showed pH 7.41, base excess − 4.1 mmol/litre, $P\text{CO}_2$ 4.0 kPa and $P\text{O}_2$ 53.5 kPa. Methaemoglobinaemia was diagnosed when it was established that methaemoglobin comprised 64% of total haemoglobin of 110 g/litre using a Co-oximeter. The other abnormal finding was a lactate 8.1 mmol/litre. Thalassaemia minor was diagnosed after evaluation of the anaemia of 110 g/litre.

The patient was referred to the medical ICU and a pulse oximeter was attached to her left index finger (Ohmeda Biox Oximeter 3700). Her measured saturation was 85% whilst receiving IPPV with 100% oxygen, before intravenous administration of 100 mg of 2% methylene blue.

Control arterial blood gases revealed pH 7.46, base excess − 3.8 mmol/litre, $P\text{CO}_2$ 3.4 kPa and $P\text{O}_2$ 56 kPa. The pulse oximeter revealed a saturation of 72% 5 minutes after injection of methylene blue, and the patient became increasingly pink. Methylene blue administration was continued up to 200 mg intravenously. The patient recovered without neurologic deficit and her trachea was extubated within a few hours. She was later questioned about possible drug consumption because examination of blood, urine, and stomach contents revealed barbiturate

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and amphetamine. She admitted that the day before admission, she cleaned her frying pan with sodium nitrite and later used the same pan for cooking supper, but denied any intentional ingestion, with the exception of an appetite supressant.

Discussion

Pulse oximetry is based on the different absorption spectra of oxygenated and reduced haemoglobin.[6] The Biox finger probe contains light emitting diodes and a photodetector which measures light absorption at two bandwidths, of 20 to 40 nm.[7]

The light absorption difference between oxyhaemoglobin and reduced haemoglobin is nearly maximal at the first bandwidth (mean wavelength 660 nm); reduced haemoglobin absorbs more red light than oxygenated haemoglobin.[6,7] At the second bandwidth (mean wavelength 940 nm), the absorption of these two states of haemoglobin vary only slightly. Analysis and computation ratio of the absorption signals in Beer's law, obtained at these two bandwidths, yields the O_2 saturation of haemoglobin in the arterial blood.[3,6,7]

Methylene blue has a spectral absorption maximum at about 670 nm, which is near the discriminating wavelength of oxygenated and reduced haemoglobin.[2,3,8] Therefore, pulse oximetry interprets the absorption by methylene blue as an increased fraction of reduced haemoglobin, with an exponential relationship to the concentration of methylene blue in the blood, and shows false low saturation values.[2-5]

Methaemoglobin and oxyhaemoglobin similarly absorb light at the wavelength of 660 nm.[9] Methaemoglobin cannot transport oxygen, although it is included in the total oxygenated haemoglobin estimation by pulse oximetry, and presents a falsely high level of saturation not proportional to the concentration of methaemoglobin.[6,7,9,10]

Our patient had a methaemoglobinaemia of 64%, apparently brought about by ingestion of unknown amounts of nitrite salts, a classical cause for methaemoglobinaemia.[11] Hence only 36% of the total haemoglobin of 110 g/litre was available for oxygen transport. Arterial O_2 content was only about 6.25 ml O_2/100 ml blood during IPPV with 100% O_2, despite an arterial oxygen tension of 56 kPa.[6] This resulted in profound hypoxaemia with complex neurological signs, abnormal respiratory pattern, and marked lactic acidosis.[11] We do not know how much the concomitant thalassaemia minor interfered with the evolution of methaemoglobin and with our measurements. The pulse oximetric saturation of 85%, measured by Biox 3700 during IPPV with 100% O_2, before treatment with methylene blue, overestimated real saturation. This occurred though underestimation of arterial saturation with the Ohmeda finger probe, the Ohmeda Biox 3700 Model 'J', and the shift of the haemoglobin–oxygen dissociation curve to the left, caused by hypocapnia and methaemoglobinaemia are taken into account.[9,11,12] The erroneous value of 85% saturation corresponds well with experimental data, of artificially induced methaemoglobinaemia of more than 60% in dogs, and measured saturation by another two-bandwidth pulse oximeter.[10]

The pulse oximetric saturation decreased to 72% 5 minutes after the administration of methylene blue, because of the interaction of this dye on light absorbance. However, simple assumptions cannot be made in this complex system of two interacting solutions, methylene blue and methaemoglobin, which is increasingly converted to haemoglobin.

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Anaesthesia, 1989, Volume 44, pages 328–331

APPARATUS

The Cyclops 33 radiation thermometer

An appraisal for use in anaesthesia

V. RAMACHANDRA, L. G. ALLAN AND F. CARLI

Summary

The Cyclops 33 is a portable infrared radiation thermometer. It has many potential advantages over existing thermometers in anaesthetic practice. The technical details are described and the benefits over other instruments discussed. This apparatus offers considerable scope for advance in the field of thermometry in anaesthesia.

Key words

Equipment; radiation thermometer.
Measurement; temperature.

Temperature is one of the six basic SI units and one of the most commonly made clinical measurements. The constancy of its normal value in homeotherms is realised in the diagnosis and treatment of local and systemic disease. Temperature has been measured since anaesthesia was first given, although the choice of instrument and sites of measurement are difficult. Most of the devices have inherent problems or can be used only in special circumstances. Thermocouples, resistance wires and thermistor probes have to be kept in continuous contact or implanted in the skin when used to measure skin temperature. This results in a mass of wiring when multiple sites are required.

The technique of infrared thermography is available for exposed skin or the outer surfaces of clothing. This has developed from use as a military tool for the location of men and machines in total darkness to a powerful medical and physiological technique with numerous applications.[1] Thermography has enabled many aspects of skin temperature distribution to be described and displayed.

Recently, a portable infrared thermometer has become available which is easy to use and provides a nearly instantaneous temperature readout. We evaluated a prototype of this new thermometer for performance and in this paper we also discuss some of its potential uses in anaesthesia.

Principle of operation

The maximum amount of radiation that can be emitted at a given temperature is known as 'black body' radiation. This is a precise known level for each wavelength, and depends only on the temperature of the emitter. No surface is a black body emitter; the ratio of the radiation emitted by a surface to that emitted by a black body at the same temperature is defined as the emissivity of the surface. It is possible to derive the temperature of a surface mathematically from a knowledge of surface emissivity, thermometer output, geometrical characteristics and spectral transmission and sensitivity.

The field of infrared thermometry is mainly concerned with emitted radiation covering the wavelengths between 0.7 and 20 μm. All infrared thermometers use selected wavebands within these limits. The Cyclops 33 (Minolta) (Fig. 1) is designed for temperature measurements from − 50 to 1000°C (− 50 to 1800°F). It is the only 'low' temperature portable radiation thermometer which offers a through-the-lens sighting system. The instrument uses a mirror system to focus the radiation onto a pyroelectric detector. Radiation from the object is focused by the optical system through a light chopper onto the detector which converts the radiation into analogue electrical signals. The detector output signal is boosted by an amplifier and fed into an A/D converter. The analogue signal is converted into a digital output and microprocessed with reference to the emissivity setting (Figs 2 and 3). According to the mode i.e. measuring (continuous, peak or valley) or calculating (mean, minimum or maximum), the output is fed to the display and digital output socket. The temperature is displayed digitally in the viewfinder and is also available for a printer, data-logger etc.

Design details

The Cyclops 33 can be powered by an internal battery or

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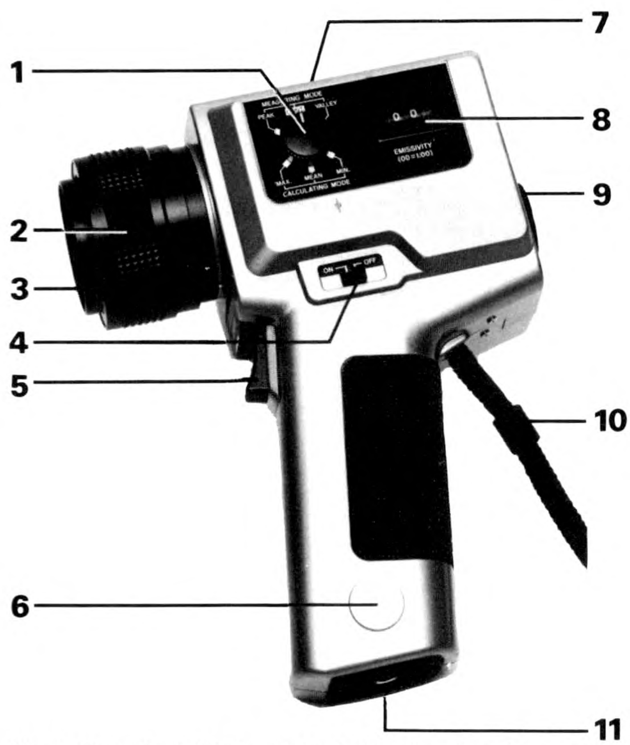

Fig. 1. Controls: 1. Mode switch; 2. Focusing ring; 3. Protective filter; 4. Power switch (on/off); 5. Trigger switch (on/off); 6. Digital output socket cover; 7. Battery compartment cover; 8. Emissivity control; 9. Eye piece; 10. Wrist strap; 11. Tripod mounting screw hole.

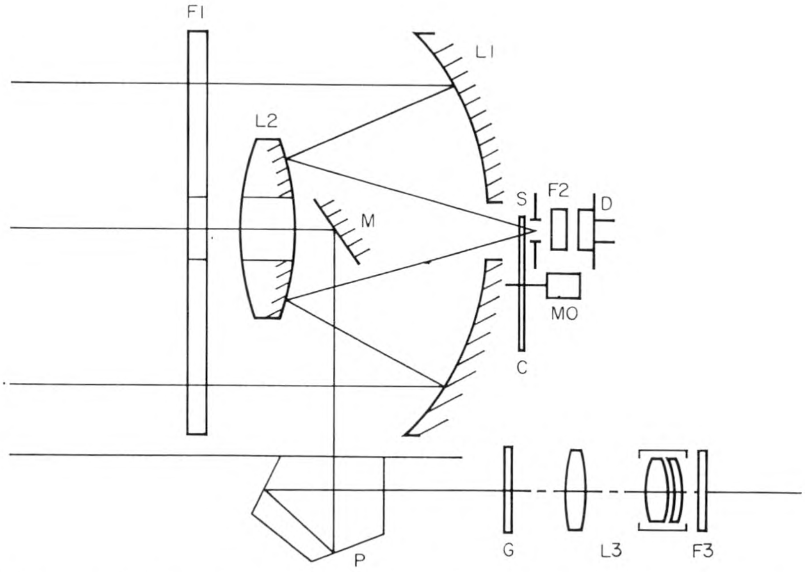

Fig. 2. Optical principle: F1, protective filter; L1, object mirror; L2, object lens; M, mirror; C, chopper; D, pyroelectric element; P, pentaprism; G, focusing plate in finder; L3, optical system in finder; F3, protective filter for eye piece; MO, motor; S, aperture plate; F2, compensating filter for spectral sensitivity.

external 9 volt d.c. (nominal) power source. The digital display response time is 0.5 seconds (steady state). Results are repeatable because the thermometer is independent of the operator; repeatability is better than 0.2% of absolute temperature.

To read the correct temperature, the emissivity control must be set to the value appropriate for the surface being measured (0.5 to 1.0) for temperatures below 100°C. The temperature display is a 4-digit liquid crystal display in the viewfinder. It is capable of 0.1°C increments below 105.5°C. The display is held for 30 seconds after the trigger is released. 'Out-of-range' readings are warned by a flashing display; emissivity warning by a flashing 'E'.

Principles of calibration

A liquid bath or standard black body surface is used for high precision calibration of low temperature radiation thermometers over the range of 20 to 200°C. The system includes a stainless steel tank with an integral heater-pump and a black body cavity. A thermometer jacket is mounted in front of the cavity and provides a fast and accurate alignment of infrared thermometers. Distilled water is used for calibration in the range of 20 to 60°C and silicone fluids for higher temperatures.

When the set temperature is reached the output from the thermometer under test is compared with the temperature reading from a National Physics Laboratory (NPL) mercury-in-glass thermometer.

System performance

The system can be tested *in vitro* and *in vivo* for its accuracy, repeatability, reproducibility, stability and response time. The accuracy of the device was ascertained *in vitro* with a stirred water bath. The bath temperature was monitored with a precision National Physics Laboratory mercury-in-glass thermometer. The *in vitro* calibration was performed over a range of clinical temperatures between 30 and 38°C and compared with a thermocouple used in clinical practice (Comark Lab).

The mean accuracy of the infrared thermometer was 0.13°C and that of the thermocouple was 0.08°C. The mean standard deviation was never more than 0.15 for the infrared thermometer at any measured temperature. (Table 1).

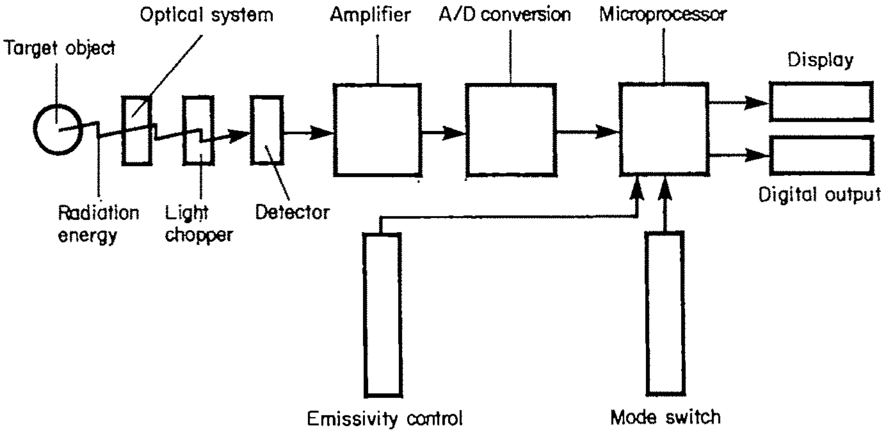

Fig. 3. Block diagram of radiation thermometer.

Table 1. *In vitro* calibration.* Values are expressed as mean (SD).

NPL thermometer (°C)	30.0	32.0	34.0	36.0	38.0
Thermocouple (°C)	30.1 (0.05)	32.0 (0.05)	33.9 (0.06)	36.1 (0.09)	38.1 (0.10)
Infrared camera (°C)	30.1 (0.07)	32.3 (0.15)	34.1 (0.09)	36.1 (0.12)	38.1 (0.12)

* Comparison with the temperature recorded by a National Physics Laboratory mercury-in-glass thermometer.

The clinical performance of the infrared thermometer was assessed by obtaining 47 measurements of skin surface temperature with either a thermocouple (used as a reference measurement) or the infrared thermometer. Excellent correlation was shown between these two measuring devices ($p < 0.008$) (Fig. 4). No significant difference was found between the infrared thermometer and the thermocouple when skin surface measurements were obtained in ambient temperatures of either 18°C, 23°C or 27°C.

The repeatability of the instrument was 0.2% of absolute temperature measured and considered satisfactory for clinical use. The measurements of surface temperature were reproducible within 30 seconds and the mean difference between two readings taken at 30-minute intervals was 0.08 (SD 0.1°C) and were not significant. The precision of focusing a point did not alter the reading. The instrument was stable for the 6-month period.

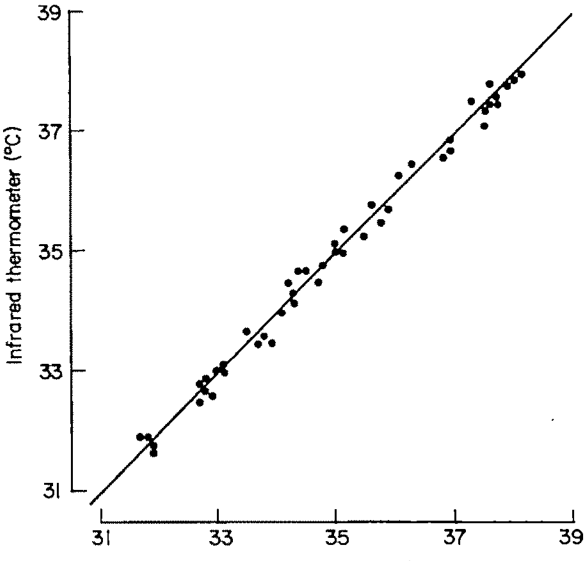

Fig. 4. *In vivo* calibration–regression line for 47 skin surface temperature measurements with the infrared thermometer and thermocouple.

Calibration is recommended every year. The Cyclops 33 reads targets as small as 5 mm accurately at temperatures above 0°C. Its wavelengths of operation minimises the effects of water vapour, carbon dioxide and sunlight.

Discussion

It appears from our evaluation that the portable infrared thermometer can measure surface temperatures reproducibly and accurately over a wide clinical range (30–38°C). This infrared thermometer offers a number of advantages over the conventional thermocouple and thermistor probes used in current clinical practice. It provides an almost instantaneous reading, has an infinite life and high sensitivity; it does not need to be in contact with the skin surface and therefore cross infection cannot occur. Other available clinical thermometers (e.g. glass–mercury thermometers, thermistors and electronic thermometers) are all contact thermometers. They must either be cleaned and resterilised between uses or employ disposable probe covers.[2] However, the two drawbacks of the device are its cost (about £2000) and the need for exposure when skin temperature measurements are made.

Recently an infrared tympanic thermometer for measuring core temperature has been evaluated and found to be accurate. The temperatures measured correlated very well with temperatures as measured by the thermistor tip of a pulmonary artery catheter in ICU patients.[3]

The possible applications of infrared thermometry both in anaesthesia and intensive care are numerous, from assessment of regional blockade to early detection of septic and cardiovascular disorders in intensive care. The technique could be of value in pain clinics and obstetric units to establish and confirm successful blocks i.e. epidural blocks, lumbar chemical sympathectomy, regional sympathectomy etc. Finally, this instrument could prove valuable as a research tool in the study of thermoregulation in anaesthetised patients.

Acknowledgments

The authors thank Land Infra-red Ltd. (UK) for supplying the Cyclops 33 (Mintola) used in this appraisal. Thanks also go to Mrs P. Smith for help with the preparation of this manuscript.

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Anaesthesia, 1989, Volume 44, pages 332–334

APPARATUS

A Kynar piezoelectric film respirometer

J. T. B. MOYLE

Summary

This paper describes a new technique for measuring respiratory gas flows and volumes using polyvinylidene fluoride film.

Key word

Equipment.

The Wright Respirometer has stood the test of time as a simple method of assessing exhaled tidal volume and minute volume of spontaneously and mechanically ventilated patients. However a number of investigators have compared its accuracy and repeatability with other flow measurement devices[1,2] and have found its accuracy is poor: one has to rely on the flow characteristics of respiration to balance positive and negative errors. It is also mechanically delicate and difficult to sterilise.

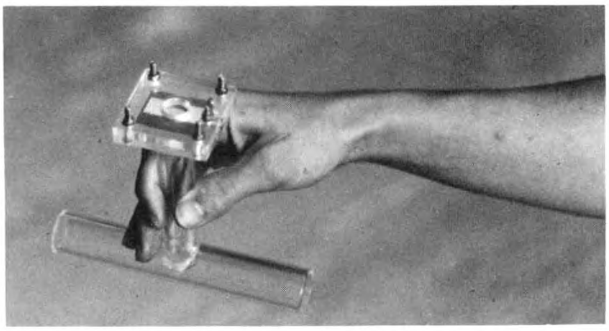

Fig. 1. The Kynar flow transducer.

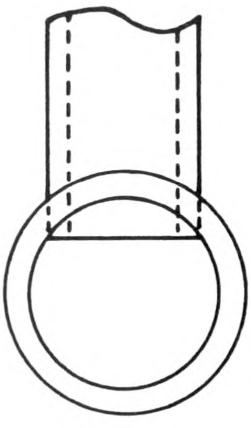

Fig. 2. View through inlet of flow transducer.

This paper describes a new technique for measuring respiratory gas flows and volumes, which makes possible the disposal of the components in contact with the patient and patient's exhaled gases.

Physical principles

Figure 1 shows the prototype transducer. Gases flow along a smooth bore tube so that laminar flow should occur. Another tube, the distal end of which is occluded, is welded at right-angles to the main tube and presents a small obstruction (Fig. 2). Turbulence occurs in the side tube as the gas flow is disturbed; the dimensions of the side tube are chosen to prevent resonance occurring in the flow range of interest. It may be shown experimentally that the amplitude of the pressure disturbance is the square of the flow passing along the main tube. The pressure changes in the side tube are measured with a pressure transducer with a high frequency response. The side tube is mounted at right angles to the main tube so that any water condensing there is not retained.

Disturbances in the respirometer's side tube are measured by occluding the side tube with a piezoelectric strain gauge made from polyvinylidene fluoride (PVDF) film. Polyvinylidene fluoride is a long chain semicrystalline polymer of the repeat-unit CH_2–CF_2, patented and manufactured by the Pennwalt Corporation of the USA and sold under the trade name Kynar.

Cady[3] defined piezoelectricity as an electrical polarisation produced by mechanical strain in certain crystals; the

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polarisation is proportional to the amount of strain and changing sign with it.

Signal processing

The low level signal from the PVDF film transducer is first amplified by a charge amplifier using an FET Op-Amp. This first stage is close to the PVDF inside a die-cast aluminium box which effectively screens the transducer from electromagnetic interference. The low impedance output from the pre-amplifier, which is a raw AC signal with a wide band width of high frequencies, is then passed through a precision AC to DC converter and a low pass filter. The signal is then taken through a square-root circuit to the integrator (Figs 3 and 4).

Results

The lowest detectable flow is 2 litres/minute. The maximum measurable flow is limited by the ratio of the diameter of the side tube to its length. This ratio must be chosen so that resonance does not occur in the working range of flows. A ratio of 1:7.5 was chosen in this case, which allows a maximum flow rate of 100 litres/minute. One disadvantage of this type of flowmeter is that it is sensitive to density and viscosity of the gas. This means that it has the characteristics of a mass flowmeter, and indicates the actual quantity of a gas or gas mixture, rather than a volume-flowmeter which indicates flow and is not affected by gas composition. This is demonstrated in Figure 5, where the output of the integrator is plotted against tidal volumes measured with a positive displacement meter, which is a volume (rather than a mass) measuring device. The tidal volumes were generated with a Manley MPP minute volume divider ventilator, using air, oxygen, and nitrous oxide.

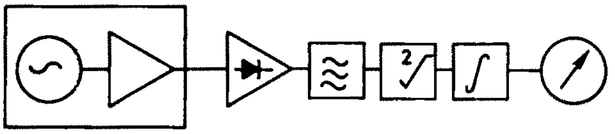

Fig. 3. Block diagram of respirometer.

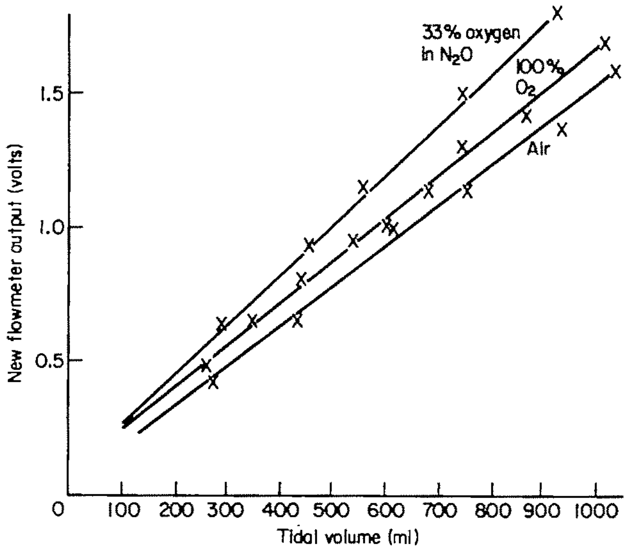

Fig. 5. Graph that shows output from integrator for air, oxygen and oxygen with nitrous oxide.

One disadvantage of this technique is microphony or the inherent sensitivity of the transducer to sound and vibration. A further development to eliminate or at least reduce this problem is to use a second transducer, identical to the first, mounted adjacent to it to detect disturbances that occur in the tube. This second piece of PVDF film has an identical pre-amplifier and precision AC to DC converter. The two signals, the one generated by the gas flow and the other caused by mechanical interference, are then passed in phase with each other through a differential amplifier which subtracts the interference signal from the flow signal.

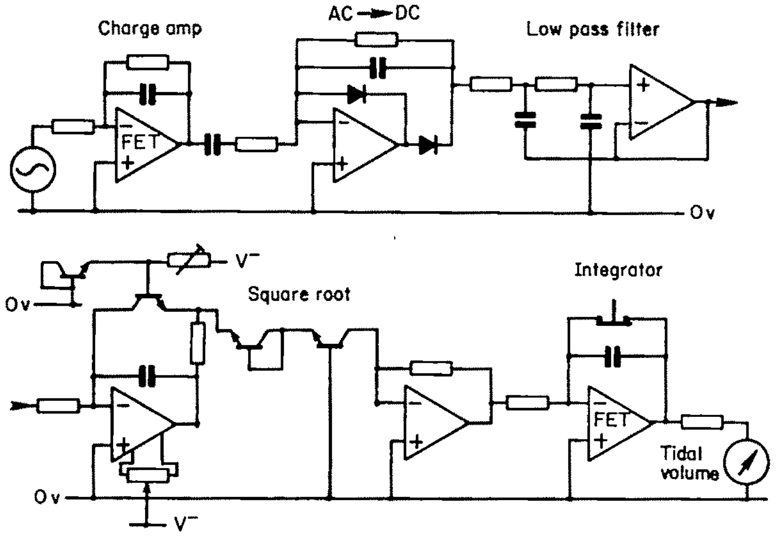

Fig. 4. Schematic circuit of respirometer.

Conclusions

This new technique to measure respiratory gas flows should be developed further because it offers: simple construction of the flow transducer, by injection moulding of plastic, which may lead to the manufacture of a disposable item and avoid the necessity of sterilisation between patients; cheapness: the price of Kynar piezoelectric film makes disposability economical. Manufacturing tolerance of Kynar film means that calibration of each flow transducer head would be unnecessary.

The disadvantages of this new technique are that it is a mass flow measuring device and with the present design of flow transducer, direction of gas system is not detectable, nor can it be used inside a gas system since changes in gas pressure will upset the calibration. However, in the majority of situations respirometers are used at atmospheric pressure. It would be possible to equalise the pressure on both sides of the transducer if this flowmeter were to be used in a closed system. Kynar film is also thermo-electric and calibration may change with changes in ambient temperature, although little effect has been detected within the range of accuracy required in clinical use.

Acknowledgments

I thank Mr S. Strachan of The Pennwalt Corporation, 74 Great King Street, Edinburgh, who holds the patent for the measurement of wind speed using this technique.

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APPARATUS

Measurement of the flow-resistive properties of double-lumen bronchial tubes *in vitro*

M. CHIARANDA, A. ROSSI, G. MANANI, O. PINAMONTI AND A. BRASCHI

Summary

This study measures the resistance to gas flow of different double-lumen bronchial tubes used for separate ventilation of each lung in critically ill patients. Different-sized Robertshaw and Carlens' tubes were studied, as well as a new device that consisted of a cuffed bronchial catheter introduced through a standard tracheal tube. The pressure-flow relationship was curvilinear in all cases. Robertshaw and Carlens' tubes were generally found to have bronchial and tracheal channels with almost similar resistance and offered total resistances similar to those of 7.0–8.0 mm internal diameter tracheal tubes. The new device had a higher resistance than others of equal external diameter. This must be taken into account when its use is recommended for prolonged respiratory support.

Key words

Equipment; tubes, bronchial.
Airway; resistance.

Knowledge of the flow resistance of tracheal tubes (TT) is needed for a rational approach to the clinical management of critically ill patients who require mechanical ventilation of the lungs.[1] It is necessary to subtract the resistance of different-sized tubes from total airflow resistance, in order to measure the patient's respiratory resistance. This information is useful in monitoring the progress of the disease as well as the effects of therapeutic manoeuvres, for example, bronchodilators, suction, or PEEP.[2–4] Furthermore high flow resistance tracheal tubes adversely affect respiratory mechanics by increasing the respiratory work of the spontaneously breathing patients, contributing to weaning difficulties[5] and slowing expiration leading to PEEP.[6–8]

A few studies have measured the pressure-flow relationships of TT,[2,4,9] and have provided a theoretical understanding of fluid dynamic factors involved in such measurements.[10,11] However, even less information exists[12] on the resistive properties of double-lumen tubes which are extensively used during anaesthesia for thoracic surgery, but are also employed when differential ventilatory modes are advisable for the treatment of unilateral lung diseases in the intensive care unit.[13,14]

A new method of separate ventilation for one-lung anaesthesia during thoracic surgery has been recently introduced by Nazari and colleagues.[15] It is based on selective bronchial intubation by means of an appropriate cuffed tube inserted through a TT. Ventilation is carried out separately through the bronchial tube on one side and the residual lumen of the ETT on the other. Successful results obtained using this new method in a number of surgical operations suggested its application for intensive care patients.

This study was undertaken to measure and compare the pressure-flow relationships of different sized double-lumen tubes whose characteristics could indicate their use for long-term ventilatory support.

Methods

Three of each of the following double-lumen tubes have been studied: left-sided Robertshaw (National Catheter Co.) sizes 37, 39, and 41 French catheter gauge (FG); Carlens' (Rusch; rubber catheters) sizes 37, 39, and 41 FG; the new device (Portex) introduced by Nazari and coworkers, manufactured in two sizes: the larger was a 5.5-mm internal diameter cuffed bronchial tube inserted through a 10-mm internal diameter TT whose outer size was similar to that of 39-FG left Robertshaw and and Carlens' tubes; the smaller was a 5-mm internal

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diameter cuffed bronchial tube inserted through a standard 9-mm internal diameter TT; outer size approximated to 37-FG left Robertshaw and Carlens' tubes.

The length and the sizes of different double-lumen tubes are reported in Table 1. To estimate an 'effective' mean inner diameter of each lumen of Carlens' and Robertshaw tubes, whose cross-sectional shape is mostly semi-oval, we closed each channel at its tip and carefully measured the amount of water necessary to fill it; the 'effective' inner diameter was then calculated from volume and length of the corresponding cylinder. The inner diameter of the tracheal lumen of the new device (i.e. the interstice between inner tracheal tube wall and outer bronchial tube wall) was calculated by subtracting the total cross-sectional area of the bronchial tube from the inner area of the tracheal tube.

All tubes were bent to exactly 90° at the elbow, in order to approximate their position in the clinical use, and were positioned (inflating their cuffs) into a Y-shaped larger tube, whose dimensions have been chosen to simulate trachea (20-mm diameter) and main bronchi (14-mm diameter).

The resistance to flow included that of 2-cm long cone-shaped connectors whose internal diameter at the most distal part was equal to the diameter of the respective tube lumina. Resistances were measured by blowing constant airflows through each channel and respective simulated bronchus, connected to a bell spirometer by a smooth tube of 20 mm internal diameter and 100 cm in length. Measurements were made at seven steady airflows, ranging from 0.125 to 1.0 litre/second.

Differential pressures were recorded between a lateral pressure tap positioned just before the cone-shaped connector and a lateral pressure tap in bronchi-sized tubes, 1 cm beyond the end of each channel (the resistance of 1-cm length of the bronchi-sized tubes was found to be insignificant).

The constant flow was calculated from the slope on the calibrated bell spirometer.

Results

The pressure-flow relationship of the tubes was curvilinear and fitted the following equation coefficient of correlation, $r = 0.999$ for all tubes:

$$P = a\dot{V}^b \qquad (1)$$

where P is the drop in pressure (kPa) needed to overcome the tube airflow resistance, a is the pressure at $\dot{V} = 1$ litre/second and b is a dimensionless number which describes the shape of the curve; $b > 1$ and $b < 1$ indicates an upward and a downward concavity of the curve, respectively (Fig. 1).

Table 2 shows the values of a and b for each channel of the double-lumen tubes used in this study and their total resistance at 1 litre/second; the latter was calculated using the formula $1/a = 1/a' + 1/a''$, where a' and a'' are the a values of bronchial and tracheal lumina, respectively.

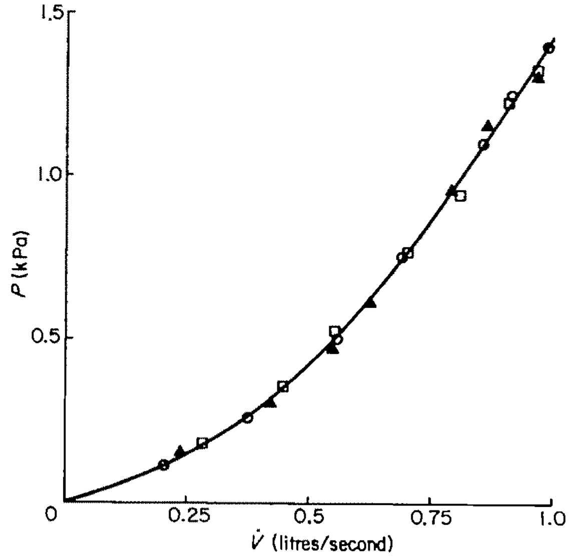

Fig. 1. Pressure-flow relationship of a representative tube, obtained on the bronchial lumen of three different left-sided 37-FG Robertshaw catheters. Different symbols are experimental data points of measurements in the three tubes. The continuous line was drawn by regression analysis and fitted the power function $P = a\dot{V}^b$, where P is the pressure value (kPa) to overcome the tube airflow resistance; a is the pressure at $\dot{V} = 1$ litre/second (1.429), and b is a dimensionless number that describes the shape of the curve (1.73). $b > 1$ indicates the upward concavity. $r = 0.999$.

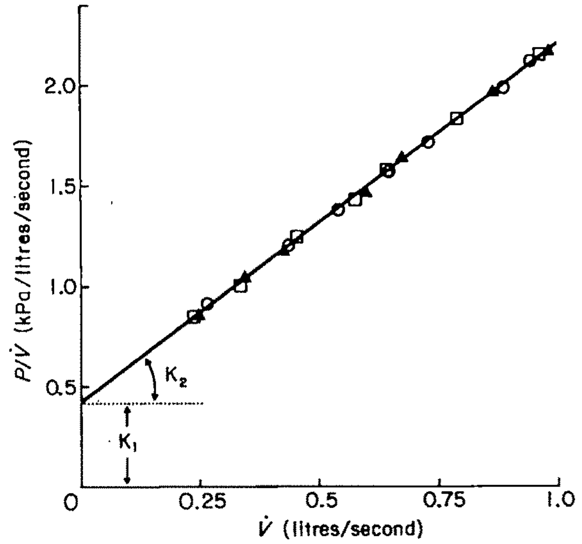

Fig. 2. Graphical analysis of K_1 (0.418) and K_2 (1.736) of a representative tube obtained on the bronchial lumen of three different 37-FG Carlens' catheters. Different symbols are experimental data points of measurements in the three tubes. The continuous line was drawn by regression analysis on the data according to Rohrer's equation. $r = 0.999$.

The pressure-flow relationships was also fitted by the classical Rohrer's equation,

$$P = K_1\dot{V} + K_2\dot{V}^2 \qquad (2)$$

which was originally proposed to describe the resistive properties of the respiratory system in humans, and then used to compute flow resistance of TT.[2] To achieve K_1 and K_2 values, we divided both sides of equation (2) by $\dot{V}$, obtaining the linear function:

$$P/\dot{V} = K_1 + K_2\dot{V} \qquad (3)$$

Table 1. Measures of tested double-lumen tubes. Total cross-sectional area available for gas flow.

Tubes	Length (cm)	Inner diameter (mm)	Outer diameter (mm)	Area (mm sq)
Carlens'				
37 FG bronchial	36	6.10	13.21	56.3
tracheal	31	5.97		
39 FG bronchial	38	6.52	14.00	65.1
tracheal	32	6.46		
41 FG bronchial	39	7.75	15.12	89.3
tracheal	32.5	7.32		
Left-sized Robertshaw				
37 FG bronchial	42	7.06	13.05	75.8
tracheal	36.5	6.83		
39 FG bronchial	42.5	7.38	14.00	84.6
tracheal	37	7.30		
41 FG bronchial	42.5	7.47	14.32	88.0
tracheal	37	7.69		
Nazari 9 + 5 mm internal diameter				
Left bronchial	48	5.00		
Right bronchial	49	5.00	13.30	46.9
Tracheal	35	5.90		
Nazari 10 + 5.5 mm internal diameter				
Left bronchial	48	5.50		
Right bronchial	49	5.50	14.00	60.4
Tracheal	35	6.84		

Table 2. Pressure-flow relationship of different double-lumen tubes (including connectors), according to the power function $P = a\dot{V}^b$. Correlation coefficient $r = 0.999$ for all tubes. Total resistance was calculated according to $1/a = 1/a(\text{bronchial}) + 1/a(\text{tracheal})$.

Tubes		Bronchial lumen		Tracheal lumen		Total resistance at $\dot{V} = 1$ litre/second
		a	b	a	b	
Carlens'						
37 FG		2.145	1.68	2.273	1.65	1.104
39 FG		1.565	1.78	1.619	1.75	0.796
41 FG		0.700	1.84	1.159	1.71	0.436
Left-sided Robertshaw						
37 FG		1.429	1.73	1.575	1.76	0.749
39 FG		1.050	1.77	1.251	1.89	0.571
41 FG		0.986	1.70	0.832	1.75	0.451
Nazari						
9.0 + 5.0 mm internal diameter	Left	6.041	1.75	5.983	1.62	3.006
	Right	6.010	1.73	5.983	1.62	2.998
10.0 + 5.5 mm internal diameter	Left	3.808	1.85	5.419	1.63	2.237
	Right	4.186	1.76	5.419	1.63	2.362

Table 3. Values of K_1 and K_2 of double-lumen tubes.

Tubes		Bronchial lumen			Tracheal lumen		
		K_1	K_2	r	K_1	K_2	r
Carlens'							
37 FG		0.418	1.736	.999	0.472	1.802	.997
39 FG		0.243	1.321	.996	0.318	1.302	.997
41 FG		0.071	0.630	.996	0.208	0.951	.999
Left-sided Robertshaw							
37 FG		0.220	1.210	.999	0.208	1.366	.997
39 FG		0.197	0.848	.999	0.094	1.157	.999
41 FG		0.198	0.786	.999	0.143	0.688	.999
Nazari							
9.0 + 5.0 mm internal diameter	Left	0.657	5.383	.991	1.326	4.667	.998
	Right	0.711	5.287	.998			
10.0 + 5.5 mm internal diameter	Left	0.394	3.415	.998	1.219	4.201	.996
	Right	0.546	3.640	.997			

and used regression analysis on our experimental points (Fig. 2). Values of K_1 and K_2 of the different double-lumen tubes are shown in Table 3.

Data were compared with results from previous studies on standard TT,[4,9] from which the following power function was obtained ($r = 0.999$):

$$a = 3105.\mathrm{ID}^{-4.14} \qquad (4)$$

where a is the pressure (kPa) at $\dot{V} = 1$ litre/second, and ID is the inner diameter (mm) of the tracheal tubes (Fig. 3). Hence we attempted to assess whether the values obtained on double-lumen tubes agreed with those

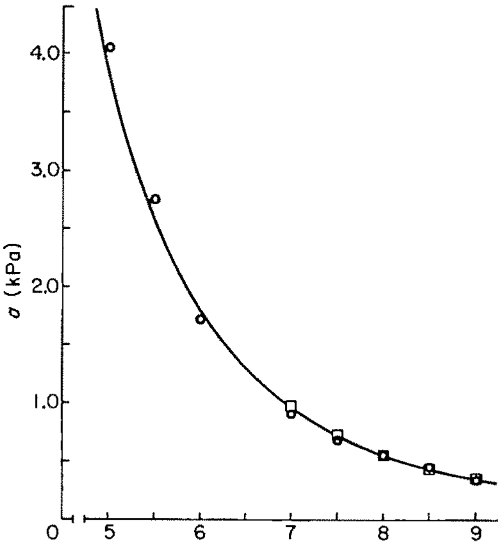

Fig. 3. Relationship between a values and inner diameter (ID) of different sized standard TT, 24-cm long, obtained by Rossi *et al.*[4] (□) and by Chiaranda *et al.*[9] (○). The continuous line was drawn according to regression analysis on data and fitted the power function. a = pressure measured at a flow of 1 litre/second.

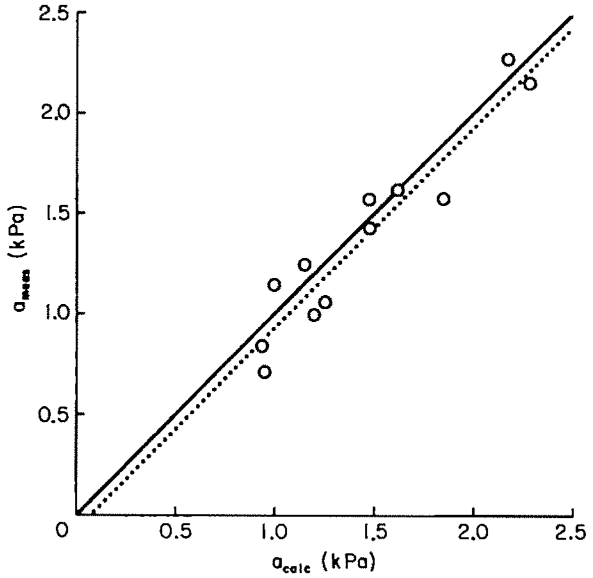

Fig. 4. Relationship between a values (open circles) measured in different double-lumen tubes, and values calculated according to equation (4) (see text). The continuous line is the identity line; the dotted line was computed by regression analysis. $r = 0.950$.

Table 4. Inner diameter (mm) of standard TT (32-cm long) with a values corresponding to those of double-lumen tubes.

Double-lumen tubes	TT
Carlens'	
37 FG	6.75
39 FG	6.95
41 FG	8.1
Left-sized Robertshaw	
37 FG	7.1
39 FG	7.5
41 FG	8.0
Nazari	
9 + 5 right	5.1
9 + 5 left	5.1
10 + 5.5 right	5.4
10 + 5.5 left	5.35

calculated according to equation (4). The latter was found to be valid in the calculation of the a value of tubes 24-cm long (plus 2-cm cone-shaped connectors), and the actual resistance (a') of each catheter of different lengths (1) was obtained as follows:

$$a' = 1.a/26 \qquad (5)$$

assuming that variations in channel resistances were directly proportional to their length, other factors being unchanged, and independently from differences in the cross-sectional shape of the tubes. The linear regression analysis on measured values (a_{meas}) and those calculated in that way (a_{calc}), fitted the equation in Figure 4.

The approximate inner diameter of standard TT whose resistances at $\dot{V}$ = 1 litre/second (a) correspond to those of double-lumen tubes was also calculated from equation (4) (Table 4).

Discussion

Left-sided Robertshaw and Carlens' tubes were designed to have tracheal and bronchial channels that offer similar resistances. Our results show small differences between the pressure-flow relationship of tracheal and bronchial channels of each tube; the bronchial lumen offers less resistance than the tracheal (except for the 41-FG left Robertshaw). Furthermore, Robertshaw tubes were designed to have a larger internal diameter than that of Carlens' tubes (overall size being equal). This was verified in our study in 37-FG and 39-FG Robertshaw channels, whose resistance was about 30–50% lower than Carlens' tubes with the same outer size. However, the bronchial lumen of the 41-FG left Robertshaw offered greater resistance than that of the 41-FG Carlens' tube.

Results show some differences in flow resistive properties between left Robertshaw and Carlens' tubes of several sizes, and between bronchial and tracheal lumena of each tube. These differences in clinical practice should not cause any particular problem for selective lung ventilation during general anaesthesia. However, when used in intensive care patients with unilateral pulmonary disease, the increase in respiratory resistance from Robertshaw and Carlens' tubes must be taken carefully into account. There is a potential risk of worsening the patient's respiratory mechanics because of pulmonary hyperinflation, with adverse effects on haemodynamics and weaning procedure, intrinsic PEEP, and increased breathing effort. The knowledge of each tube's partial and total resistances at different flows is essential to compute the patient's intrinsic respiratory resistance under these circumstances (Tables 2 and 3).

Hammond and Wright[12] made a detailed comparison of the resistances of double-lumen tubes bent to 90° at the elbow and found resistances significantly lower than those obtained in our study. Some reasons can be advanced to explain these differences.

We used constant airflows to simulate mechanical lung

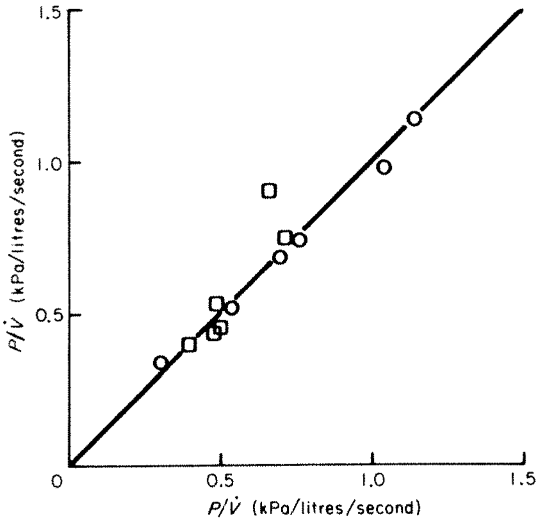

Fig. 5. Relationship between values of different-sized double-lumen tube resistances reported by Hammond and Wright[12] (ordinate), and values obtained in this work at $\dot{V} = 0.35$ litres/second (abscissa). Open circles are data measured on 37-, 39-, and 41-FG Carlens' tubes; open squares are data obtained on 37-, 39, and 41-FG left-sided Robertshaw catheters. Continuous line is the identity line.

inflation. The catheters were inserted into a larger tube that represented the trachea and main bronchi, to avoid the potential artefact stressed by Chang and Mortola[11] during measurement of TT resistance in isolation. The validity of this method was assessed and supported by Behrakis and colleagues,[2] who showed that the pressure-flow relationship of TT was independent of the direction (inspiratory or expiratory) of a continuous flow. This condition was also verified in our previous experiment *in vitro* on TT.[9] Hammond and Wright in their study used a sinusoidal airflow of 50-ml tidal volume delivered at 3 Hz by a cylinder pump: some differences between data obtained using continuous airflows or the forced oscillatory technique might be taken in account, because ventilatory frequency may influence the measurement of catheter resistance, other factors being equal.[11] Furthermore, Hammond and Wright[12] measured the pressure at the proximal end of the channels, presumably ending freely to the atmosphere; if the tubes were without connexion to a trachea-sized tube, the dissipation of kinetic energy at the abrupt cross-sectional area-change, from the tube to the atmosphere, could have increased the resistance of the channels.[10,11] More likely however, the difference between the results might be explained by assuming that those authors measured resistances at a flow of about 0.35 litres/second (the flow at which resistance was measured is not quoted in their paper). If resistance values reported in Table 3 are calculated at a flow of 0.35 litres/second according to Rohrer's equation, then the sample data points of both studies are almost the same (Fig. 5).

A single number cannot describe the flow resistance of the tubes, because of the curvilinear $P/\dot{V}$ relationship over a wide range of flows. This is in agreement with previous observations[2,4,9] and has important implications for comparison between patients, and even for assessment of changes in respiratory mechanics for the same patient. The large increase in pressure with increasing flow, indicates that measurement of total resistance in mechanically ventilated patients can be significantly influenced by the size of the tracheal or bronchial tubes as well as by the mode of ventilation.

Our data show a good correlation with results of previous experiments performed on standard TT (Fig. 4), which showed that the mostly semi-oval cross-sectional shape of bronchial and tracheal channels has little influence on the resistance they would have offered if the cross-sectional area had been circular throughout their length. Small and medium sized double-lumen tubes offer total resistance significantly higher than TT commonly used for prolonged ventilatory support in patients with respiratory failure.

Surprisingly, we found that the cross-sectional area of the device described by Nazari and his colleagues[15] was smaller than that of double-lumen tubes with nearly similar outer size (Table 1).

This explains why the 5-mm internal diameter bronchial catheter offered resistances 2.5–4 times greater than those created by bronchial channels of 37-FG Carlens' (6.0 mm internal diameter) and Robertshaw (7.1 mm internal diameter) tubes, respectively. In the same way, 5.5-mm internal diameter tubes offered a similar increase in resistances in comparison with bronchial lumena of 39-FG Carlens' (6.4 mm internal diameter) and Robertshaw (7.4 mm internal diameter) tubes.

The differences in sectional area between the tracheal channels of the tubes tested were less, but the turbulence of gases flowing through the gap between tracheal and bronchial catheters of the new device considerably increased its flow-resistance, from theoretical values of 2.75 and 1.53 kPa at a flow of a litre/second [calculated according to equation (4) for smaller and larger sizes, respectively], to measured values of 5.98 and 5.42 kPa. Hence, the tracheal lumen of the new device created resistances 3–4 times greater than those offered by tracheal channels of Carlens' and left Robertshaw tubes of similar outer size. This does not cause any problems during anaesthesia for thoracic surgery, according to the clinical experience of Nazari *et al.* where the authors were satisfied that the new method was superior to the use of conventional double-lumen catheters. However, it seems less suitable for prolonged ventilatory support.

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Forum

Epidural fentanyl and perineal pain in labour

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Summary

Perineal pain during the course of routine epidural analgesia with bupivacaine was treated with a 10-ml top-up of either bupivacaine 25 mg, fentanyl 100 µg or fentanyl 100 µg plus bupivacaine 10 mg, in 46 women in the first stage of labour. Only fentanyl plus bupivacaine produced consistently reliable analgesia which was quicker in onset and longer in duration (140, SD 26 minutes) than either fentanyl (114, SD 26 minutes) or bupivacaine (99, SD 44 minutes) alone. Side effects, itching and drowsiness, which were not troublesome, were more frequent in the groups given fentanyl.

Key words

Analgesics, narcotic; fentanyl.
Anaesthetic techniques, regional; epidural.

Epidural fentanyl, 80 µg, has been shown to produce good analgesia when added to the bupivacaine test dose in the first stage of labour.[1–3] However, when used only at the beginning of labour, it reduces bupivacaine requirement only for the first dose, and its use has not been associated with an overall reduction in side effects or instrumental delivery rate.[1–3] Walton and Reynolds[4] found, in a retrospective survey, that perineal pain treated with epidural bupivacaine 0.5% was associated with an increased instrumental delivery rate. Epidural fentanyl might be better able than low dose bupivacaine to cure perineal pain in labour, since solution placed in the lumbar epidural space is better sited to reach the sacral segments of the cord than to reach the sacral roots in the epidural space. Also, as it causes only nociceptive block, it should be less likely to inhibit the bearing down reflex.

The present study was designed to explore the value of fentanyl in the treatment of perineal pain in the course of a bupivacaine epidural, by randomised single-blind controlled trial.

Method

Mothers were included in the trial, after ethical approval and informed consent, if they had a singleton cephalic presentation and reported perineal pain during the first stage of labour in the presence of epidural blockade of T_{11-12} that produced warm, dry feet and uterine analgesia. They were allocated randomly to receive one of three treatments through the epidural catheter, in a semi-sitting position. One group received bupivacaine 25 mg, another fentanyl 100 µg and a third fentanyl 100 µg plus bupivacaine 10 mg, all made up to 10 ml with physiological saline, termed the index dose. Pain was assessed on a 10-cm visual analogue scale before administration of the index dose and 10, 20 and 30 minutes after. The time of the first painless contraction was recorded. Supplementary doses were given if the patient requested it, until she was satisfied.

The occurrence of a 20% change in systolic arterial blood pressure, nausea, vomiting, itching, leg weakness, and fetal heart changes were noted during the first 30 minutes after the index dose. Further top-ups were given at the mother's request. If perineal pain recurred when the initial treatment of perineal pain had been successful, it was repeated. Alternative treatment was given if the index dose was unsuccessful.

Each mother completed a questionnaire on the first post partum day, that related to her recollection of pain relief and side effects. The differences between the groups were assessed using Student's *t*-test or Fisher's exact test.

Results

Clinical data are given in Table 1. There were no significant differences in age or parity, though the greater number of primipara in the fentanyl/bupivacaine group was associated with a significantly longer epidural duration than in the fentanyl group ($p < 0.05$).

Pain relief. Analgesia was satisfactory in all women in the fentanyl/bupivacaine group after the index dose, but in the other two groups supplements were required in some cases to achieve satisfactory pain relief (Table 2). Of the five women in the bupivacaine group in whom perineal pain returned later, three were given bupivacaine again and in all it was successful. In the other two, in whom bupivacaine had not previously given satisfactory analgesia, fentanyl and bupivacaine were given next time round and were successful. Five women in the fentanyl group with good analgesia from the index dose, received further fentanyl on recurrence of perineal pain but it was never successful second time round, and all of these and two others in whom fentanyl had been unsuccessful required the addition of bupivacaine. By contrast in the fentanyl/bupivacaine group, further doses of the two drugs were successful seven times out of seven for the next dose. Altogether 41 doses of

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Table 1. Clinical data.

	Bupivacaine	Fentanyl	Bupivacaine/ fentanyl
n	16	14	16
Primipara	9	8	11
Age, years, mean (SD)	27.6 (5.3)	28.5 (6.2)	26.7 (6.0)
Labour induced	13	5	11
Syntocinon augmentation at time of index dose	13	5	10
Cervical dilatation at time of index dose, cm, mean (range)	5.7 (2–10)	4.8 (2–10)	5.69 (1–10)
Perineal pain score before index dose, cm, mean (SD)	6.06 (1.6)	4.32 (1.8)	5.40 (1.6)
Total epidural duration, minutes, mean (SD)	333 (120)	272 (94)	425 (225)
Index dose — delivery, minutes, mean (SD)	196 (106)	197 (81)	283 (190)

Table 2. Further dose requirements.

	Bupivacaine	Fentanyl	Bupivacaine/fentanyl	p values
n	16	14	16	
Number that required supplements to achieve satisfactory analgesia	6	2	0	Bupivacaine compared with fentanyl/bupivacaine: 0.017
Number that required further top-up for perineal pain	5	8	7	
Number that required different treatment for perineal pain	2	7	0	Fentanyl compared with fentanyl/bupivacaine: 0.0024

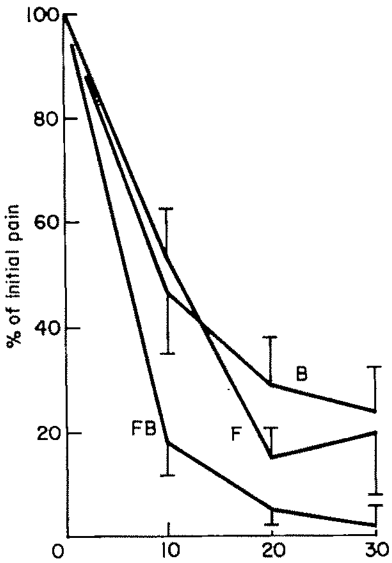

Fig. 1. Mean pain scores presented as percent of initial pain in the three treatment groups. B, bupivacaine 25 mg; F, fentanyl 100 μg; FB, fentanyl 100 μg + bupivacaine 10 mg. Vertical lines represent standard errors. At 10 minutes FB score is significantly better than B and F ($p < 0.02$). At 20 and 30 minutes FB score is significantly better than B ($p < 0.05$).

fentanyl/bupivacaine were given and all produced satisfactory pain relief.

Pain scores decreased most rapidly after the index dose, and were lowest at 30 minutes in the fentanyl/bupivacaine group (Fig. 1). Onset of analgesia (determined as the time to achieve a painless contraction) was significantly quicker, and duration (time to next top-up) significantly longer in the fentanyl/bupivacaine group than in either of the other two (Table 3). There is always a proportion of patients who, despite apparently completely satisfactory analgesia, do not record a pain score of zero.

Side effects. Side effects after the index dose are reported in Table 4. Leg weakness, though never marked, was not avoided in the fentanyl/bupivacaine mothers. Hypotension was not severe in any group. Itching occurred in just over half the women given fentanyl, but was not a serious complaint in any case. Nausea was not common, but numbers were not consistent with those in the patients' questionnaire. Shivering was not reported in any group. The fetal heart pattern remained unchanged following the index dose in the majority of cases (Table 5), with no significant difference between the groups.

Outcome. There was no significant difference in the number of spontaneous deliveries or in the one minute Apgar scores in any group (Table 6).

Patients' assessment (Table 7). The majority of women in all groups reported that pain relief had been satisfactory in the first stage of labour, but 25% who received bupivacaine alone, 33% given fentanyl and bupivacaine and 50% given fentanyl alone reported it to be fair or unsatisfactory at delivery. This difference was not significant. There was no significant difference between the groups in the numbers who reported nausea and vomiting, but a significantly larger number of women who had received fentanyl said they had been drowsy ($p < 0.05$). This was particularly noticeable in the fentanyl/bupivacaine group compared to those who received bupivacaine alone ($p < 0.02$).

Discussion

Perineal pain, which is transmitted by roots S_{2-4}, is generally remarked by parturients only when the pain of uterine contraction (T_{11-12}) is successfully eliminated by lumbar epidural blockade. The numbers in this study are not large, because of the selection criteria and because as the trial proceeded, it seemed unethical to withhold the combination treatment, with its clear advantages. Bupivacaine 25 mg produced satisfactory anaglesia by itself in only 63% of cases, and onset of complete analgesia was slow. Fentanyl 100 μg by itself was successful in 83% of index doses, but it was never successful when repeated. Only the combination produced analgesia which was 100% successful on initial and repeat administration and it was, moreover, significantly quicker in onset and longer in duration than either fentanyl or bupivacaine alone. The trial was not double-blind, but the patient was unaware of her treatment and supplements and top-up doses were given only at her request.

Morphine, whether given intrathecally or epidurally in the management of labour pain, produces analgesia of poor quality with a high incidence of side effects.[5–11] After epidural pethidine in labour, analgesia is brief and at least partly attributable to local anaesthetic effect.[12,13] This is not, of course, a characteristic specific to pethidine, but

Table 3. Onset and duration of analgesia, minutes. Values expressed as mean (SD).

	Bupivacaine	Fentanyl	Bupivacaine/ fentanyl
Onset			
(time to pain-free contraction)	23.7 (16.0)	19.2 (7.0)	10.4 (4.8)
n	13	9	11
Duration			
(time to next top-up)	99.0 (43.8)	114 (26.8)	140 (26.5)
n	7	12	10

Onset: FB compared with B, $p < 0.02$; FB compared with F, $p < 0.01$. Duration: FB compared with B, $p < 0.05$; FB compared with F, $p < 0.05$.

Table 4. Side effects recorded during 30 minutes after the index dose.

	Bupivacaine	Fentanyl	Bupivacaine/ fentanyl
n	16	14	16
>20% fall in systolic pressure	2	1	1
Itching	0	8	8
Nausea	0	1	2
Leg weakness*			
mild/moderate	4	0	10
severe	4	0	0

* Mild/moderate, able to raise knees with difficulty; severe, unable to lift legs off the bed.

Table 5. Fetal heart changes after index dose.

	Bupivacaine	Fentanyl	Bupivacaine/fentanyl
n	16	14	16
Unchanged	10	11	14
Deteriorated	2	2	2
Improved	4	1	0

Table 6. Delivery type and Apgar score.

	Bupivacaine	Fentanyl	Bupivacaine/ fentanyl
Spontaneous vertex	10	6	10
Instrumental vaginal	5	8	5
Caesarean section	1	0	1
Apgar score <7 at 1 minute	2	2	1

Table 7. Retrospective assessment by patient.

	Bupivacaine	Fentanyl	Bupivacaine/ fentanyl
n	16	14	15*
Pain relief during labour/at delivery (L/D)			
	L/D	L/D	L/D
Satisfactory	15/12	11/7	15/10
Fair	1/3	2/4	0/3
Unsatisfactory	0/1	1/3	0/2
Side effects			
Nausea	5	4	3
Vomiting	3	0	1
Drowsiness	6	9	13

* One mother did not complete a questionnaire.

simply a reflection of its low potency as an opiate agonist, that necessitates a dose large enough to have an unselective effect. Epidural butorphanol may be associated with an undesirable degree of somnolence both during labour[14] and after Caesarean section.[15]

Fentanyl, by contrast, has consistently been found to produce satisfactory epidural analgesia in labour,[1–3,16–18] though its duration of action is only marginally longer than that of bupivacaine and the hope that it might eliminate or reduce the need for bupivacaine has not been fulfilled in practice. More recently, alfentanil epidural infusion[19] and sufentanil in various doses added to epidural bupivacaine[20–22] in labour have had modest success, but with no striking advantages.

Fentanyl 100 μg produces less prolonged epidural analgesia than diamorphine in the postoperative period,[23] but there is no advantage in increasing the dose of fentanyl.[24] Diamorphine, however, does not block labour pain reliably (personal observation), so interest in fentanyl persists, and discussion has centred on optimising the concentration of fentanyl and the relative doses of fentanyl and bupivacaine. Arcario and colleagues[25] showed that fentanyl 50 μg should be dissolved in 10 ml or more of saline for best results after Caesarean section, and most workers use about 10 ml for analgesia. Rucci *et al.*[26] added 50, 100 or 200 μg to 20 ml of 0.5% bupivacaine in surgical patients, with no conspicuous advantages. This is hardly surprising since 100 mg of bupivacaine works well by itself. For pain relief, as opposed to surgery, it is clearly more appropriate to see what dose, if any, of bupivacaine should be added to fentanyl, if the local anaesthetic-induced motor and sympathetic blockade are to be minimised. There is evidence that the presence of local anaesthetic potentiates fentanyl analgesia after Caesarean section,[27] which is certainly borne out in the present study in which analgesia from fentanyl alone was less reliable, slower in onset and briefer in duration than that after fentanyl plus bupivacaine 10 mg.

Cohen and her colleagues[16] examined various combinations of bupivacaine and fentanyl, but did not include a group given no bupivacaine. They found that bupivacaine 22.5 mg alone produced more frequent hypotension and emesis than combinations, that bupivacaine 7.5 mg with fentanyl 100 μg was less successful than bupivacaine 22.5 mg with fentanyl 50 or 100 μg, but that the larger dose of fentanyl was associated with more motor block after top-ups than any of the other treatments. We have found smaller doses than 22.5 mg of bupivacaine to be effective with fentanyl in the past (12 mg + 80 μg) and in the present study (10 mg + 100 μg). The difference is explicable in the present study in that the dose was given in the course of an established bupivacaine epidural. Motor block also occurred in our combination group, but it was less profound than in the group given bupivacaine only in whom the bupivacaine dose was larger (25 mg).

Shivering, often a problem during the onset of epidural analgesia in obstetrics, may be suppressed by epidural opiate.[28] Shivering was not observed in this study, which was started in each case *after* the establishment of the epidural block. Almost all women who had been given the combination treatment reported drowsiness retrospectively, but this was not apparent to the observers during labour, and was therefore presumably less severe than the somnolence that accompanied butorphanol.[14,15]

Grice *et al.*,[17] who used bupivacaine 25 mg plus fentanyl 50 μg in labour found that the mean duration of analgesia with adrenaline 37.5 μg (180 minutes) was significantly longer than without (137 minutes). This is consistent with the present findings for the combination (10 mg + 100 μg) without adrenaline, but when this work is compared with others' it must be borne in mind that the index dose was given in late labour when top-up durations are commonly shorter than in early labour when the other trials were conducted. Chestnut and colleagues[18] also used rather large doses of bupivacaine with fentanyl by bolus and infusion, and found that the combination worked better than bupivacaine alone, though with no great advantage and in particular no improvement in normal delivery rate. The normal delivery rate of 62.5% in the combination group in our series, was the same as with bupivacaine alone, with no advantage when plain fentanyl was used in the index dose.

It is clear therefore that epidural fentanyl provides good analgesia in labour when combined with bupivacaine, but that it is pointless to add it to a dose of bupivacaine which would be effective on its own. Present and earlier work suggests that, in combination with fentanyl, as little as 10–12 mg of bupivacaine suffice. But even with this low dose there is no clear reduction in side effects, which are not troublesome with bupivacaine 0.25% alone. Throughout all the trials the only consistent significant difference in side effects between epidural opioids and local anaesthetics is the frequency of pruritus. With fentanyl, however, this is not troublesome. There is, moreover, no dramatic improvement in normal delivery rate.

We believe, however, that one clear indication for epidural fentanyl is in the treatment of perineal pain, which is commonly more intractable than abdominal pain when bupivacaine is used. Also, it may require much larger doses that result in marked leg weakness, undesirable in the first stage of labour. When fentanyl 100 μg is used with bupivacaine consistent perineal analgesia is produced and so larger bupivacaine doses can always be avoided.

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Pulse oximetry in the recovery room

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Summary

Haemoglobin oxygen saturation (So_2) was measured percutaneously with a pulse oximeter, in a group of 150 healthy ambulant volunteers to determine the range of normal values. The measuring site was not arterialised in advance. So_2 was below 94% in 13.3% of cases, while in no case was it below 90%. So_2 was then measured in 350 patients in the recovery room after a variety of surgical and anaesthetic procedures. Only 1.1% of patients who received additional oxygen following general anaesthesia exhibited an So_2 below 90%, compared to 16.7% of similar cases who did not receive additional oxygen. Administration of additional oxygen raised the So_2 above 90% in all the latter cases. In only 55.3% of those who did not receive additional oxygen was the So_2 above 94%, compared to 86.7% of normal volunteers and 73.9% of patients who received additional oxygen. This study reiterates the need to administer supplemental oxygen to all patients in the recovery room, unless facilities are available to measure So_2. A lower alarm limit of 90% is appropriate for the peri-operative period when using the Criticare Systems 501 oximeter.

Key words

Equipment; pulse oximeter.
Hypoxia; postoperative.

The principles behind pulse oximetry have been known for 50 years,[1] but it is only recently that a new generation of pulse oximeters has developed which are small and simple enough for routine clinical use. Pulse oximeter saturation estimations (So_2) correlate well with saturations measured directly from simultaneous arterial blood samples.[2,3] The apparatus is gaining widespread acceptance as a peri-operative monitor, especially when arterial desaturation commonly occurs.

However, pulse oximetry is known to be an unreliable estimate of Sao_2 in certain situations;[4,5] the main one is hypoperfusion at the measuring site. There is little information in the literature about the normal range of So_2, but it has been suggested that during anaesthesia and recovery So_2 should be greater than 94–95%, to correspond to a theoretical Pao_2 of 10 kPa.[5] However, another report[6] defines hypoxaemia as an So_2 less than 90% when using the Nellcor device; this corresponds to a theoretical Pao_2 of 8 kPa.

This study was designed to answer: what is the range of So_2 in the normal population; what is the range of So_2 measurable in patients in the recovery room; can the pulse oximeter be employed reliably in the recovery room, without preparation of the measuring site beforehand as an indicator of the need for oxygen therapy; is routine administration of additional oxygen necessary in the recovery room?

Methods

Throughout this study So_2 was measured using the same Criticare Systems 501 pulse oximeter. The standard adult finger probe was employed and applied following the manufacturer's instructions. No special preparation of the skin was carried out before measurement. Saturation estimations were made when the display reading had stabilised, after a 30-second warm-up time had been allowed. A failure was recorded if a saturation reading was not obtained after four attempts on different digits.

One hundred and fifty ambulant adult volunteers were studied in the first investigation. All were hospital staff in ASA grade 1, between the ages of 19 and 59 years, who had been working in a room temperature above 20 °C for at least 2 hours. None was receiving vaso-active medication or had been engaged in strenuous activity immediately before the study. The measurement was made at rest with the volunteer breathing quietly; the finger to which the pulse oximeter probe was attached was selected at random and held at waist level. The volunteer was instructed not to move the finger during the determination. Volunteers were asked to indicate whether they were smokers or not. The lower limit for So_2 found during this investigation was taken as the reference lower limit of the normal range for the Criticare 501 oximeter and employed in the rest of the study.

For the second investigation 350 adult patients aged 16–84 years and in ASA grades 1–3 were studied in the recovery room 15–30 minutes after a variety of surgical procedures under either regional or general anaesthesia. Patients were in one of three groups, depending upon their situation in the recovery room as they presented for study: Group 1, general anaesthesia, no additional oxygen given in the recovery room (150 patients); Group 2, general anaesthesia, oxygen 2 litres/minute via a nasopharyngeal catheter in the recovery room (100 patients); Group 3, regional anaesthesia, no additional oxygen given in the recovery room (100 patients).

Allocation to a particular study group was therefore

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not randomised; the need for oxygen therapy was determined on clinical grounds by the anaesthetist in charge of the case, but was not under the authors' control. Oxygen was administered through a 12Ch. fenestrated nasopharyngeal catheter which did not incorporate a foam nostril plug.

Patients were only included in the study if they fulfilled the following criteria: haemodynamic stability, with a mean arterial blood pressure above 50 mmHg; axillary temperature above 35 °C; recovery room staff, all with special ICU training and experience, were satisfied with the condition of the patient.

Measurements were not made if the recovery room temperature was below 20 °C. Again, the finger to which the pulse oximeter probe was attached was selected at random; if the operation site was on the arm then the contralateral arm was selected for saturation measurements. Smoking history was also noted. If the recorded saturation was below 90% in patients not receiving additional oxygen, oxygen at 2 litres/minute was given through a nasopharyngeal catheter and the measurement repeated after 5 minutes had elapsed.

Results

Demographic details of the study groups are shown in Table 1. Thirty-eight of the 150 volunteers were smokers (25.3% of the total). Figure 1 shows the scatter of saturation measurements; 20 (13.3%) lie below 94% saturation, and in this subgroup five of the volunteers (25%) were smokers. None of the volunteers exhibited an So_2 below 90%. There was no correlation between So_2 and age ($y = 0.01x + 95.9$, $r = 0.07$).

The mean arterial pressure was above 70 mmHg and within 20% of the pre-operative value in all of the patients studied. Figures 2–4 show the scatter of So_2 measurements in the different groups. There were eight measurement failures (2.3% of the total number); all occurred in patients in Group 2 (8% of this group). Table

Table 1. Demographic details of the study groups.

	Mean age, years (SD)	Sex		ASA category		
		M	F	1	2	3
Volunteers	32.4 (9.3)	75	75	150	0	0
Group 1	41.9 (15.9)	77	73	106	36	8
Group 2	56.5 (18.3)	44	56	42	36	22
Group 3	53.1 (16.2)	68	32	65	27	8

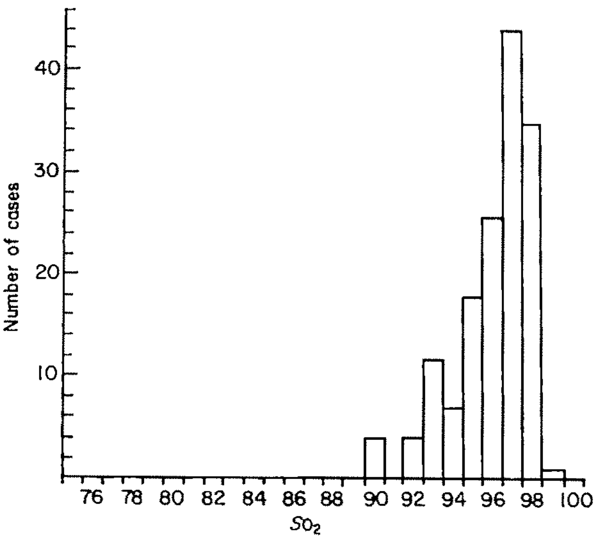

Fig. 1. Saturation measurements in 150 ambulant volunteers.

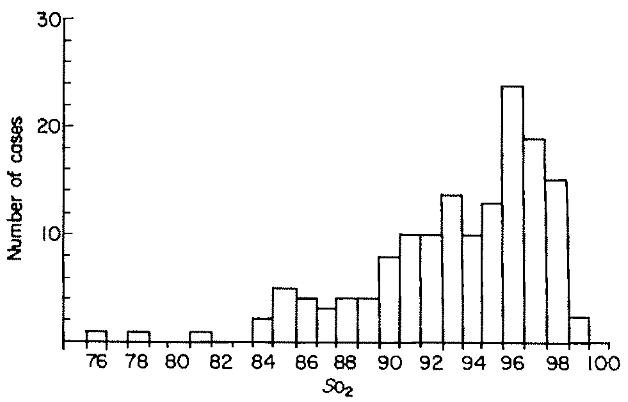

Fig. 2. Saturation measurements in 100 patients after general anaesthesia; no additional oxygen was given in the recovery room.

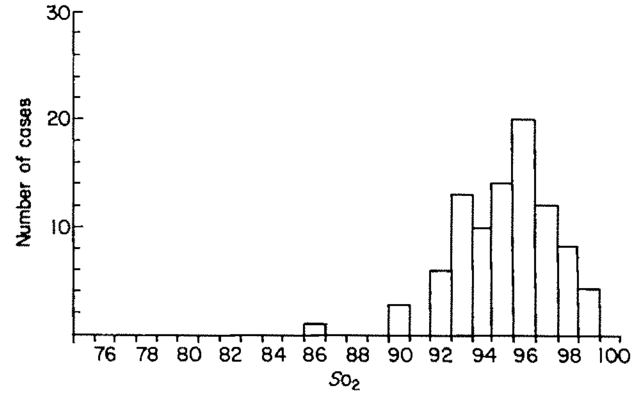

Fig. 3. Saturation measurements in 100 patients after general anaesthesia; oxygen 2 litres/minute was given in the recovery room.

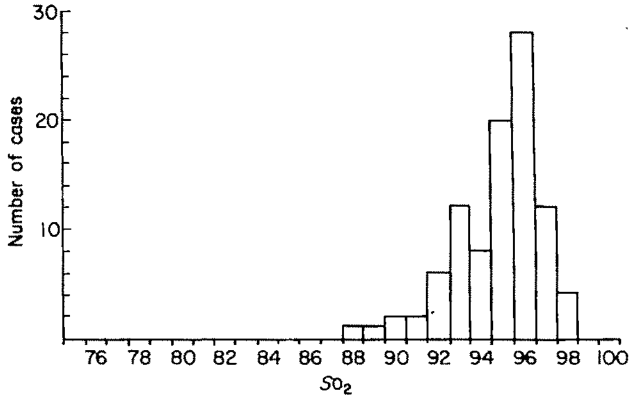

Fig. 4. Saturation measurements in 100 patients after regional anaesthesia; no additional oxygen was given in the recovery room.

Table 2. Characteristics of the patients in Group 2 in whom an So_2 was unrecordable.

Patient	Age	Sex	ASA status	Operation
1	63	M	2	Aortobifemoral bypass
2	74	F	1	Cholecystectomy
3	85	F	1	Hip hemiarthroplasty
4	43	F	1	Oophorectomy
5	63	F	3	Renal transplant
6	28	F	3	CAPD catheter
7	67	F	1	A–P resection
8	68	M	3	Heel debridement

Table 3. Characteristics of patients in Group 1 who exhibited an So_2 below 90%.

Patient	Age	Sex	Smoker	ASA status	So_2	Operation
1	62	F	No	1	89	Microlaryngoscopy
2	38	M	No	1	89	Orchidopexy
3	21	M	No	1	89	Mandibular osteotomy
4	58	M	No	1	89	Excision neuroma neck
5	48	M	No	1	88	Rectopexy
6	68	M	No	2	88	Retropubic prostatectomy
7	63	M	No	2	88	Subcapsular orchidectomy
8	60	F	No	1	88	Retinal detachment
9	23	F	No	1	87	Zygoma fracture
10	28	F	No	1	87	Laparoscopy and dye test
11	36	F	Yes	2	87	Lumbar fistulectomy
12	68	M	No	2	86	Lymph node biopsy neck
13	66	M	No	1	86	Dynamic hip screw
14	45	M	No	2	86	Hemigastrectomy
15	35	F	No	1	86	Genioplasty
16	50	M	No	1	85	Elective appendicectomy
17	14	F	No	1	85	Staging laparotomy
18	54	F	No	1	85	Varicose veins
19	25	F	No	1	85	Urethral dilatation
20	60	F	No	1	85	Mandibular osteotomy
21	37	M	Yes	1	84	Herniorrhaphy
22	57	F	No	2	84	Abdominal dehiscence
23	53	F	No	1	81	Exploratory laparotomy
24	43	F	No	1	78	Parotidectomy
25	28	F	No	1	76	Laparoscopy

2 lists these patients and their associated conditions. There was no detectable effect of age, ASA status, or smoking habit on postoperative So_2.

Sixty-seven patients (44.7%) in Group 1 exhibited an So_2 below 94%. In 25 patients (16.7%) So_2 was under 90% (Table 3), but after the administration of oxygen, So_2 increased above 90% in all patients and above 94% in 17 patients.

Twenty-four patients (26.1%) in Group 2 exhibited an So_2 below 94%, while in only one case was So_2 below 90%. The patient was a 26-year-old man who underwent a 6.5-hour operation for peripheral fracture fixations after multiple trauma. Increasing oxygen flow to 5 litres/minute resulted in an So_2 of 93%. In Group 3, 24 patients exhibited an So_2 below 94%, while in only two patients was the So_2 under 90%. Administration of oxygen brought the So_2 values up to 93% and 95% respectively.

Discussion

This study sheds some interesting light on the use of pulse oximetry in anaesthesia. In the volunteer group, 13.3% exhibited an So_2 less than 94%, the lower alarm limit suggested by Taylor and Whitwam,[5] while none of them exhibited an So_2 below 90%. The accuracy of So_2 measurements, when compared with co-oximeter readings, is purported to have been demonstrated for situations in which peripheral perfusion is adequate.[2,3,7] However, the statistical method used to assess agreement may be inappropriate,[8] and a recent study indicates that So_2 readings may depend upon venous as well as arterial blood volume in the measured tissue.[9] So_2 and Sao_2 may therefore be different but related quantities.

We only encountered measurement failures in patients in Group 2. Our failure rate compares favourably with that quoted by Mihm and Halperin[7] who found a failure rate of 22% when pulse oximetry was used in intensive care patients. There is confusion in the literature as to whether arterialisation of the measuring site is necessary.[3,10] We made no attempt to improve local perfusion at the measuring site during this study. It is possible that the use of heat, vasodilator creams or friction may have allowed a reading; further work needs to be done using oximeters which display a pulse waveform in order to evaluate this technique. It is not current policy in this hospital to administer additional oxygen in the recovery rooms. Consequently the patients in Group 2 were 'sicker' than those in Group 1 (Table 1), and this may account for the high measurement failure rate in this group.

We did not perform a randomised study, nor did we use controlled inspired oxygen fractions, since this investigation was initiated as a study of current practice in our institution. However, in only one case out of a total of 127 patients who were given oxygen was the So_2 below 90%. This occurred in a young patient following a lengthy procedure for the repair of multiple fractures, in whom the hypoxaemia was readily reversed by increasing the oxygen flow rate. This figure contrasts markedly with the 16.7% of patients who exhibited an So_2 below 90%, after general anaesthesia when no additional oxygen was given in the recovery room. This is in spite of more patients from Group 2 who were in ASA category 3. Postoperative hypoxaemia has been recognised for 25 years,[11] but it is not certain whether this is detrimental to the patient. Many normal subjects exhibit mild arterial desaturation during sleep,[12] but assuming that iatrogenic desaturation is undesirable, this study indicates that all patients should be given additional oxygen in the recovery room unless facilities are available to measure So_2. Interestingly, two of the patients operated upon under regional analgesia exhibited an So_2 below 90%. The first case (So_2 89%) was a 37-year-old woman who suffered from severe rheumatoid arthritis. She underwent a synovectomy at the wrist under brachial plexus anaesthesia and received no sedatives during the procedure. Postoperative chest X ray excluded pneumothorax, but widespread opacification was demonstrated, consistent with rheumatoid lung disease. The second case (So_2 88%) was a 63-year-old man who received a total hip replacement under epidural anaesthesia in combination with sedation using midazolam. In both these cases the hypoxaemia was readily reversed with additional oxygen.

In the recovery room, So_2 readings may be adversely affected by the vasoconstriction produced by hypothermia, hypotension, pain and the use of vasopressors. Patients with high bilirubin levels[5] and those to whom particular dyes (methylene blue, cardiogreen) have been administered[4] may exhibit falsely low So_2 values. This latter may have been the explanation for the low So_2 value in patient 10 in Table 3; she received a large quantity of methylene blue during a laparoscopic dye test.

A falsely high So_2 reading may be found in heavy smokers and patients exposed to carbon monoxide. All but one of the currently available pulse oximeters fail to distinguish between HbO_2 and COHb because only two wavelengths of light were utilised to determine So_2. After 12 hours' abstention from smoking COHb levels and P_{50} values return to normal, even in moderate smokers.[13] This means the effect of CO on So_2 may be negligible in light to moderate smokers who have elective surgery. However, the use of pulse oximetry in heavy smokers, especially those who have emergency surgery, and patients in the acute phase of a burn injury, may be inadvisable.

In conclusion, we find the Criticare Systems 501 pulse oximeter to be a reliable monitor of postoperative oxygenation, although the addition of a pulse waveform display would be a useful guide to the state of peripheral perfusion. We consider that in routine use a lower alarm limit for So_2 of 90% should be employed in the recovery room. Further work is required to determine whether a higher alarm limit may be more appropriate for other machines, or when arterialisation of the measurement site is carried out.

Acknowledgments

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Carbon dioxide—a survey of its use in anaesthesia in the UK

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Summary

A random postal survey of 1528 anaesthetists in the UK was performed to assess their use of carbon dioxide in anaesthesia and opinion on its safety. Of 1100 replies (72% response rate), 60.9% used it daily and 77.1% would object to its exclusion from future anaesthetic machines. There was no consistent age-related trend with regard to its use or opinion on its removal. 62.9% of anaesthetists did not regard its presence on the anaesthetic machine as hazardous, but 81.8% agreed that a limit to the maximum flow of carbon dioxide delivered to one litre/minute would improve safety.

Accepted 6 May 1988.

Key words

Carbon dioxide.
Equipment; anaesthetic machine.

Carbon dioxide (CO_2) was first used in anaesthesia in 1824 by Henry Hill Hickman, who performed a series of operations on animals and used it to produce 'suspended animation'.[1] Leak and Waters[2] used 30% CO_2 in oxygen to produce unconsciousness in humans in 1928. Marked ventilatory and circulatory stimulation, rigidity and convulsions rapidly ended its investigation as an inhalational anaesthetic agent.

The ability of CO_2 to stimulate ventilation at lower concentrations was probably instrumental in Boyle's inclusion of a delivery system for CO_2 on his anaesthetic apparatus in 1927.[3] It has remained since then, a common feature of anaesthetic machines in the UK, despite the increasing use of normocapnoeic controlled ventilation and the use of the capnometer in modern practice.

This survey was performed to determine to what extent, and for what purposes carbon dioxide is used in clinical practice in the UK, and to gauge opinion on its safety.

Method

All hospitals in the UK which had an anaesthetist listed in the 1985 edition of *The medical directory*[4] were numbered in the alphabetical order in which they appeared. Two hundred were randomly selected out of a total of 657 hospitals thus listed. These hospitals were sent a letter that explained the proposed survey and requested a list of their consultants, senior registrars and registrars.

Questionnaires, with a stamped, addressed envelope for the reply, were addressed to the individuals listed, and posted with the others for that department to the chairman or consultant in charge of administration. This allowed a second opportunity to approve participation. The questionnaires were addressed to individuals, but both the anaesthetists and the hospitals at which they worked remained anonymous, because they replied separately.

The questionnaire was divided into three categories and enquired about: the anaesthetist's grade, age and whether most of their anaesthetic training had occurred in the United Kingdom; use of carbon dioxide, frequency, indications and major use; attitude to its exclusion from the anaesthetic machine, or its replacement by a system for air in machines limited to three gas delivery systems; accidents, opinion on whether its presence on the anaesthetic machine is hazardous or not; knowledge of local cases of mishaps and their worst outcome; whether decreasing the maximum flow of carbon dioxide delivered to one litre/minute would be considered safer.

A 3-month period (November 1986–January 1987) was allocated for the return of the completed questionnaires. One of the aims of the study was to ascertain whether the use of carbon dioxide was related to anaesthetic trends at the time of training and therefore the ages of the anaesthetists, so the results were divided into age categories of 41 years and over (41 +) and 40 years and under (− 40). The tabulated results were analysed using the Chi-squared test.

Results

Of the 200 hospitals randomly selected, 143 (71.5%) replied to the introductory letter that requested a list of consultants, senior registrars and registrars; 134 hospitals (67%) were suitable and nine were excluded for the following reasons: refused to participate, 1; operating theatre closed down, 2; staffed by clinical assistants or associate specialists, 6.

The anaesthetists. Questionnaires were sent to the 1528 anaesthetists listed. This represented 40.2% of the total of anaesthetic consultants, senior registrars and registrars in post in the UK in 1986. The population sampled appeared to be a representative one as the percentage of each grade sent questionnaires (Table 1) was almost identical to the distribution of grades in the UK.

Replies were received from 1100 anaesthetists (72%) by the end of the allocated period, representing 28.9% of the three grades of UK anaesthetists. The percentages show a bias in the distribution of the replies towards consultant numbers and away from registrars. Possible causes for this are a greater interest in the survey among consultants, and more registrar questionnaires mislaid because of their movement between hospitals. Nevertheless, this represented 57.6% of the questionnaires sent to registrars; since only 29 anaesthetists (2.6% of the total replies) had performed most of their anaesthetic training outside the UK, this was an insignificant influence on the overall replies.

Use of carbon dioxide. Table 2 shows the frequency with which anaesthetists used CO_2 within the age groups. There is a statistically significant ($p < 0.01$) relationship between age and usage of CO_2 but the relationship is inconsistent. Indeed, the 41 + group were more polarised in their attitudes and tended either never to use carbon dioxide, or use it several times a day compared to the −40 group.

The stimulation of spontaneous ventilation after a period of controlled hyperventilation was the most common indication (54%) for the use of CO_2 (Table 3); 71.2% regarded this as their major indication. Few thought that blind nasal intubation (16.1%) and the relief or prevention of laryngospasm (10.6%) were indications. The other uses suggested by the anaesthetists are shown in Table 4.

Anaesthetists were against the removal of CO_2 from the

Table 1. Anaesthetists surveyed and replies. Percentages in parentheses.

	Questionnaires sent $n = 1528$	Number of UK anaesthetists* $n = 3803$	Replies $n = 1100$
Consultants	952 (62.3)	2329 (61.2)	748 (68)
Senior registrars	177 (11.6)	457 (12)	122 (11.1)
Registrars	399 (26.1)	1017 (26.8)	230 (20.9)

* Number of anaesthetic consultants, senior registrars and registrars in post in UK in 1986 (personal communication with health departments).

Table 2. Use of CO_2 by anaesthetists in the month before completion of questionnaire. Percentages in parentheses.

Age group	Never	Once/week	Once/day	Several times/day
−40	96 (16)	142 (23.7)	180 (30.1)	181 (30.2)
41+	110 (22)	82 (16.4)	135 (26.9)	174 (34.7)
Total	206 (18.7)	224 (20.4)	315 (28.6)	355 (32.3)

Table 3. Use of CO_2. Percentages in parenthesis.

Age group	Indications for use				Major indication				
	(i)*	(ii)†	(iii)‡	Others	(i)*	(ii)†	(iii)‡	Others	None
−40	511 (57.6)	121 (13.6)	84 (9.5)	171 (19.3)	456 (74)	29 (4.7)	12 (1.9)	66 (10.8)	53 (8.6)
41+	385 (49.8)	146 (18.9)	92 (11.9)	150 (19.4)	350 (67.9)	31 (6.0)	13 (2.5)	62 (12.0)	60 (11.6)
Total	896 (54)	267 (16.1)	176 (10.6)	321 (19.3)	806 (71.2)	60 (5.3)	25 (2.2)	128 (11.3)	113 (10)

*, The stimulation of spontaneous ventilation after a period of hyperventilation; †, blind nasal intubation; ‡, prevention/management of laryngeal spasm.

Table 4. Other uses of carbon dioxide. Figures are the number of anaesthetists listing each use.

To maintian normocapnia during IPPV.	124
To speed up uptake during inhalation induction of anaesthesia	144
As a treatment of hiccoughs or coughing during anaesthesia	21
To manipulate $Pa\mathrm{CO_2}$ levels in ophthalmic, carotid, plastic and neurosurgery	13
Wake up tests and to speed up emergence from anaesthesia	3

Table 5. Attitudes to removal of CO_2 from the anaesthetic machine. Percentages in parentheses.

Age group	Strongly object	Slightly object	Not object	Be pleased
−40	219 (37.2)	219 (37.2)	119 (20.2)	32 (5.4)
41+	277 (58.7)	103 (21.8)	59 (12.5)	33 (7.0)
Total	496 (46.7)	322 (30.4)	178 (16.8)	65 (6.1)

Table 6. Air instead of CO_2? Percentages in parentheses.

Age group	Yes	No
−40	272 (47.8)	297 (52.2)*
41+	124 (26.8)	338 (73.2)*
Total	396 (38.4)	635 (61.6)

* Significant difference ($p < 0.01$).

Table 7. Outcome of accidents associated with the administration of CO_2. Only incidents that occurred at anaesthetists' present place of work noted. Percentages in parentheses.

Age group	None	Morbidity	Mortality
−40	31	51	26
41+	34	26	32
Total (n = 200)	65 (32.5)	77 (38.5)	58 (29.0)

anaesthetic machine; 77.1% objected and only 22.9% did not object or were pleased with its proposed removal (Table 5). Chi-squared tests suggested a statistically significant ($p < 0.01$) relationship between the age groups and these attitudes, although the actual percentages show this to be a nonlinear relationship; the 41+ group were more likely to object strongly or be pleased than the −40 group.

Table 6 shows that if anaesthetists were limited to three gas delivery systems, 61.6% would not want CO_2 substituted by an air delivery system; significantly more ($p < 0.01$) of the 41+ group objected to this suggestion.

Accidents. The number of individual incidents is not known, although 200 anaesthetists knew of an accident with CO_2 that occurred at the hospital at which they currently worked. Of these, 29% resulted in death and only 32.5% were judged as having suffered no ill effects (Table 7).

Table 8. Is CO_2 on the anaesthetic machine hazardous? Percentages in parentheses.

Age group	Yes	No
−40	250 (42.2)	342 (57.8)*
41+	154 (31.0)	343 (69.0)*
Total	404 (37.1)	685 (62.9)

* Significant difference ($p < 0.01$).

Table 9. Would it be safer to have a limit of one litre/minute on the carbon dioxide flowmeter? Percentages in parentheses.

Age group	Yes	No
−40	490 (82.6)	103 (17.4)
41+	386 (80.8)	92 (19.2)

The presence of a CO_2 delivery system was not regarded as hazardous by 62.9% of anaesthetists (Table 8); the difference between the age groups was significant ($p < 0.01$). Limiting the flow of CO_2 from a flowmeter to one litre/minute was thought by 81.8% of anaesthetist to be safer than present systems (Table 9).

Discussion

The use of CO_2 in anaesthetic practice in the UK was found to be widespread and enthusiastically defended. It should be borne in mind, in assessing the quality of the data presented, that the use of CO_2 was estimated by the anaesthetists retrospectively, and is therefore open to systematic bias, as is the whole of any postal survey which relies on voluntary information. Nevertheless, because of the size of the survey, high response rate and clearcut differences in attitudes shown, the results are probably a close approximation to the actual situation.

The stimulation of spontaneous ventilation after a period of controlled hyperventilation was the main indication for the use of CO_2. Despite attempts to avoid extreme hyperventilation in anaesthesia, some hypocapnia is common. The return of spontaneous ventilation is likely to be delayed postoperatively while the $Pa\mathrm{CO_2}$ increases since the respiratory drive is often depressed by opiates and anaesthetic agents. Ivanov and Nunn[5] found that after prolonged hyperventilation, 5% CO_2 is the most rapid and repeatable method of elevating the end-expiratory $P\mathrm{CO_2}$, compared to hypoventilation or step reduction of minute volume; furthermore it replenishes body stores of carbon dioxide. If CO_2 stores rise as a result of hypoventilation there will be consequent hypoxaemia, if the patient breathes air postoperatively,[6] and slower elimination of inhalational anaesthetic agents.

The maintenance of normocapnia during controlled ventilation and the acceleration of uptake during inhalational induction of anaesthesia were the second and third most popular uses; blind nasal intubation and prevention or management of laryngeal spasm had the fewest advocates.

Nevertheless, the UK remains one of the few countries that still orders appreciable numbers of new anaesthetic

Table 10. Deaths/cerebral damage associated with accidental hypercapnia from administered CO_2.

Author (s)	Period of collection of data	Anaesthetic related deaths/cerebral damage	CO_2 related deaths/cerebral damage
Edwards G *et al.* (1956)[10]	1950–1955	589*	2
Dinnick OP (1964)[11]	1955–1964	400*	1
Wylie WD (1975)[12]	1964–1973	66	2
Utting JE *et al.* (1979)[13]	1970–1977	348	4

* Only deaths reported.

machines with a CO_2 delivery system. Factors such as the greater use of circle breathing systems with CO_2 absorbers, reliance on nurse anaesthetists, the use of capnometers to produce normocapnoeic controlled ventilation and concern about its hazards, has dissuaded some countries from its use.

The presence of a CO_2 flowmeter on the anaesthetic machine introduces several hazards. Hypercapnia has profound physiological effects, but it is difficult to recognise on the basis of clinical observation,[7] and even severe hypercapnia is not necessarily fatal, provided adequate oxygenation is maintained.[8] However, a maximum flow of 15–20 litres/minute can be produced through a carbon dioxide flowmeter, with the needle valve fully opened and the bobbin wedged at the top,[9] so that a combination of hypoxia and hypercapnia will result. Evidence from the literature of deaths or permanent cerebral damage secondary to accidental hypercapnia from administered carbon dioxide is summarised in Table 10. All these surveys relied on voluntary reports, often with incomplete documentation, and may therefore underestimate the occurrence of significant sequelae. The incidence of minor mishaps is also unknown, although Craig and Wilson,[14] in a survey of 81 nonfatal anaesthetic misadventures, revealed one case of accidental hypercapnia out of 8312 anaesthetics in 6 months. It is therefore likely that several cases of nonfatal accidental hypercapnia may occur in the UK per annum.

Most accidents occur when the carbon dioxide flowmeter remains 'on' unnoticed[15–17] other than the rare instances of incorrectly filled gas cylinders.[18,15]. Despite this hazard, simple safety devices such as a mechanical stop on the carbon dioxide needle valve to limit the maximum flow have only recently been introduced.[9] Mechanical linkage of the nitrous oxide and oxygen flow control valves is now common but does not link to the CO_2 flow control valve. Safety in using carbon dioxide has relied upon recommendations, such as disconnexion of the cylinder when not in use, availability of 5% CO_2 in oxygen only,[20] or the use of 12-litre 'sparklet' cylinders.[8] Nevertheless, since serious mishaps with CO_2 are still reported to the DHSS[17] (the most recent case in the last 6 months—personal communication with the DHSS), it appears the hazard of accidental hypercapnia continues to be underestimated. This was illustrated by the survey in which 62.9% of anaesthetists did not regard its presence on the anaesthetic machine as hazardous, and yet 81.8% did regard limiting the maximum flow as an improvement in safety.

It is difficult to justify its continued use in such an uncontrolled manner, since no evidence suggests that either patients or anaesthetists are at a significant disadvantage by the absence of CO_2 in modern clinical practice, and that fatalities occur despite awareness of its hazards. The safest option is CO_2's withdrawal from routine clinical use since the universal use of capnometers is unlikely in the near future and the modification to limit the maximum flow of all existing flowmeters might not be feasible logistically. This survey shows that this would be an unpopular decision.

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SPECIAL ARTICLE

Anaesthesia and the law

Awareness and pain during anaesthesia

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Machine setting error responsible for failure of anaesthesia during 45-minute operation.

In 1986, Mrs Dorothy Smallwoods, a fit 31-year-old married woman (a keen runner and aerobics teacher) who was then living in Londonderry, Northern Ireland, noticed that she had 'a lump the size of a golf ball' on her clavicle. Tests indicated Hodgkin's disease and surgery was recommended; it was proposed to remove her spleen and to take biopsies from the liver, kidneys, lymph glands and other potentially affected areas.

In February 1987 she was admitted to Altnagelvin Hospital, Londonderry. She was not given a drug premedication. However, in the early afternoon she was moved from the ward to the operating theatre annexe and injected in one hand with drugs to make her drowsy and then promptly rendered unconscious by drugs infused into her other hand. Thereafter muscle relaxants were administered and an airway inserted. The oxygen bypass button was locked on. The patient, now rendered helpless, unable to speak and physically paralysed save for an occasional flutter of the eyelids, was soon to regain full mental awareness and consciousness.

Failure to notice patient's unanaesthetised condition

Two people in the operating theatre (probably students) pointed out that the patient's pupils were not dilated just before the operation began. The anaesthetist, having first delivered them a short lecture on the way anaesthetics worked, closed her eyes to prevent them from drying out. Thereafter, although the patient did try to flutter her eyelids again to try to attract the medical team's attention to her condition, it was to no avail. Indeed, shortly before the end of the 45-minute operation, it was thought that she was 'coming round', so she was given a further dose of muscle relaxant.

The patient suffered acute pain throughout the operation during which the surgeon made a 7.5-cm abdominal incision, removed the spleen and investigated the other organs, swabbed the wound and then finally stitched up the wound. It was not until she was wheeled away from the operating theatre that she was able to shout out, 'I was awake in there!'

Incorrect machine setting the cause of the error

The consultant anaesthetist on being informed of this, hastened back to the theatre to discover that the oxygen flush was locked in the 'on' position and that therefore a very dilute anaesthetic was given to this patient during the entire operation. (A Cape-Waine Mark III anaesthetic-ventilator was apparently in use.—*Editor*).

The error apparently happened after a problem which arose during the preceding operation: a patient's condition had suddenly deteriorated, oxygen had been urgently required, and, most unfortunately, the machine had not been reset.

Compensation and apology

The patient sued the hospital in negligence, accepting a 'few thousand pounds' by way of compensation in an out of court settlement after the hospital had admitted full liability for the incident. No amount of money could compensate her in her view, for the torment she had endured, although it was some small comfort that the hospital staff had immediately believed her story and she was given morphine on her return to her bed. Nobody from the hospital contacted her husband to tell him what had happened so he did not travel up to visit her until the next day. Both the surgeon and the anaesthetist did come to see her to apologise personally, but the patient was upset by the anaesthetist's initial explanation that the error lay with the machinery.

In a newspaper interview, published in September 1988, the patient said that she believed that the anaesthetist had been at fault for failing to notice and correct the error on the machine setting and that she did not wish to see him again though he did ask if he might visit her another time. She apparently felt extremely isolated and shut-in with her ordeal while she recovered in the ward. She felt unable to confide in other patients awaiting surgery, her parents and friends. She perceived the medical staff as reluctant to make eye contact with her, which depressed her. (Avoidance by medical staff of a patient injured by medical error is not uncommon, caused perhaps by guilt and embarrassment).

The machine used in the plaintiff's case has since been modified to prevent a recurrence of this sort. The patient has now successfully completed her radiation therapy. Her hair has grown back, she has regained weight, there are no signs of recurrence, and she is now able to speak of her ordeal. She has made a point of visiting the anaesthetist again and is able to accept that he appreciated the effects of the incident and regretted it deeply.

She was haunted following her ordeal, by episodes of panic and recurrent nightmares which have subsided with the assistance of psychiatric therapy. However, she remains unable to cope with stress and continues to be fearful of pain and further surgery.

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Clinical freedom and clinical behaviour

The escalating cost of medical defence surely suggests that our medical house should take stock to ensure that its affairs are fully in order. We seem often to blame the attitude of patients or the legal profession but surely it is not so much their attitude as the new awareness, such that patients or their relatives know when all is not as it should be. Clinical arrogance, protected or justified by a conviction in the mystic rights of clinical freedom, lies at the basis of many serious omissions or errors in patient care. Clinical freedom is the opportunity, guarded by our profession, to practise using the precautions that are correct and appropriate to the knowledge of the era in which we live. Clinical freedom may reasonably be compared with civic freedom and requires the same responsibility and the right to live and work within defined rules, rules defined not by the individual but by responsible authority. However it seems, by the usage of a minority, to be best described as the right to hold one's practice to be right and to claim the support of colleagues for that view, even when, by the standards of 1989, it may be shown to be patently wrong. Clinical freedom has become the cloak behind which ignorance may hide and the need to keep abreast of advances in medicine avoided. It therefore may permit practice by anecdote and whim. There are of course instances for which present information is inadequate and for which the appropriate management has yet to be described but, even so, an informed and prudent choice using conventional wisdom, but not hearsay, may be made between treatments or techniques.

If neither ignorance nor arrogance are to blame for many of the clinical disasters and near misses, then surely it is judgement that must be criticised. The time has come to accept that, in 1989, medicine is a more exact science, in so far that, apart from the planned studies designed to advance into the gloom of ignorance, strategies for the best management of many diseases or choice of techniques in surgical and anaesthetic practice are well described. There can be no excuse, not even that of ignorance, for other

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than the careful use of these. An appropriate example is the selection of the anaesthetic technique for laparoscopy; I believe the choice is obvious; the patient's airway and ventilation must be protected by tracheal intubation and intermittent positive pressure ventilation of the lungs. Some anaesthetists, I am told, neither intubate nor ventilate routinely and, by such omission in my opinion, hazard their patient.

The need to monitor has always been with us. It is the machinery for monitoring that we have lacked. The arguments abound that we are being driven to increase the degree of monitoring by the threat of litigation. This may be true but we should not be driven by self interest to avoid litigation but rather by enthusiasm to extend our awareness of the patient's state and thereby safety. Those who still argue that the educated finger is the most appropriate monitor must catch up with time and recognise that whatever its many uses the finger is only a finger and has a very limited capacity for education. The absentee landlord who spends time somewhere else needs to delegate responsibility but remains accountable for the area of his responsibility. Unfortunately, there are also absentee anaesthetists, often those who vote for the finger but who find an interest elsewhere more appropriate than a finger in the theatre. The 'common finger' can be commended provided the glue at the end is strong. The application of monitors, recommended by the Association of Anaesthetists' report, and preparation of the patient takes time, but we must remember that it is the patient and not the doctor who takes the shortcuts and the risks. It is the patient who suffers from ill informed opinion and whim, but who could also gain from the wise use of knowledge.

We must not permit Health Authorities to deny us the appropriate instrumentation. Their immediate argument is that it is new and that we did not require it before and so we must wait, that is, our patients must wait; this is no less specious than it would be if the same argument were applied to prevent the introduction of lithotripsy or the replacement of obsolete radiographic equipment by new and safe technology.

We all know the standards of practice we expect of others. Why is there so much variation in our own? Each one of us certainly knows whom we would trust, or not, to anaesthetise our own mother or spouse. It is this choice which is the most formidable peer review. Is it because we know the difference that peer review is in vogue and limited term consultant contracts a threat on the horizon? It is arrogant to claim the right to clinical freedom without an appreciation of the responsibilities that this brings. We accept, claiming the clinical freedom granted by our profession and being protected by it, the responsibility that was entrusted to us as medical students when we vowed to avoid the shortcuts, to keep abreast of our subject and to apply accepted practice. Clinical freedom for our profession proceeds from responsible behaviour by each and every individual so that it remains not only correct to defend it but ensures that it is worth defending, as the freedom to do what is right, to differentiate between the good and the bad and the freedom to choose within the limits that the body of our profession prescribe for us.

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Asystole on induction: do we monitor it?

This is a report of two cases of brief asystole on induction in the anaesthetic room. Both patients were monitored with an electrocardiograph (ECG) and pulse palpation, without which, it is suspected the asystole would not have been detected.

A fit, ASA 1 grade, 24-year-old woman, who weighed 60 kg, presented for retinal detachment surgery. No premedication was given. Routine monitoring was commenced in the anaesthetic room, before induction. This was an ECG, with a back pad electrode (Deseret Med. Inc.) and palpation of her radial pulse by a nominated nurse. Her pulse was 90 beats/minute, sinus rhythm. Anaesthesia was induced with fentanyl 75 μg, droperidol 2.5 mg, thiopentone 300 mg, and vecuronium 7 mg. The patient's lungs were then manually ventilated using a Bain system and mask with 50% oxygen, 50% nitrous oxide and enflurane 1%. Laryngoscopy was performed after 2 minutes and 100 mg lignocaine spray (Astra Pharmaceuticals) administered to the larynx and trachea.

Immediately after the completion of spraying, the nurse reported that the radial pulse was absent; this was confirmed on the ECG. The patient's trachea was intubated straightaway to secure her airway and her lungs' ventilated with 100% oxygen. Spontaneous recovery to sinus rhythm occurred rapidly over the next 15 seconds before any other specific therapy was administered, although glycopyrronium 0.3 mg was given as prophylaxis against stimulation of the oculocardiac reflex during the operation.

The rest of the anaesthetic and procedure continued uneventfully and the patient made a normal recovery.

A 58-year-old man, who weighed 65 kg presented for cataract extraction and insertion of intra-ocular lens. He smoked 20 cigarettes/day, but he had no respiratory symptoms and was generally fit and well. He had a normal chest X ray, ECG, and urea and electrolytes. A precisely similar sequence of events occurred to that described above.

It is not routine to monitor the patient in all anaesthetic rooms due to limitations of appropriate equipment and (or) staff.[1] The brief periods of asystole in these two cases, would not have been detected, without the monitoring. One suspects, however that there still would have been a satisfactory outcome since the asystole simply resolved after tracheal intubation and ventilation of the lungs, which would be the normal sequence of events.

Recently, workers who studied the cardiovascular responses to a similar induction sequence found that there was no significant change in heart rate before intubation and a significant slowing in the first 2 minutes after intubation.[2] They suggest that vecuronium has a bradycardic effect which is augmented by the addition of fentanyl. Perhaps the vagomimetic combination of fentanyl and vecuronium[2] along with laryngoscopy, sufficiently facilitated the predominance of vagal stimulation from laryngoscopy (rather than the normal balanced stimulation of vagal and cardiac accelerator fibres),[3] to cause asystole. The stimulation of intubation,[3] regardless of the presence of topical lignocaine[4] caused adequate stimulation of the cardiac sympathetic B receptors to resolve the asystole, without any further pharmacological intervention.

Cases of severe bradycardia and asystole are reported during the maintenance of anaesthesia with vecuronium as the muscle relaxant;[5] some of these were associated with surgical vagal stimulation[6] but none is described when vecuronium was used as the muscle relaxant for intubation. Is this because they are very rare, or more likely, is it because they are only transient, and in fact are

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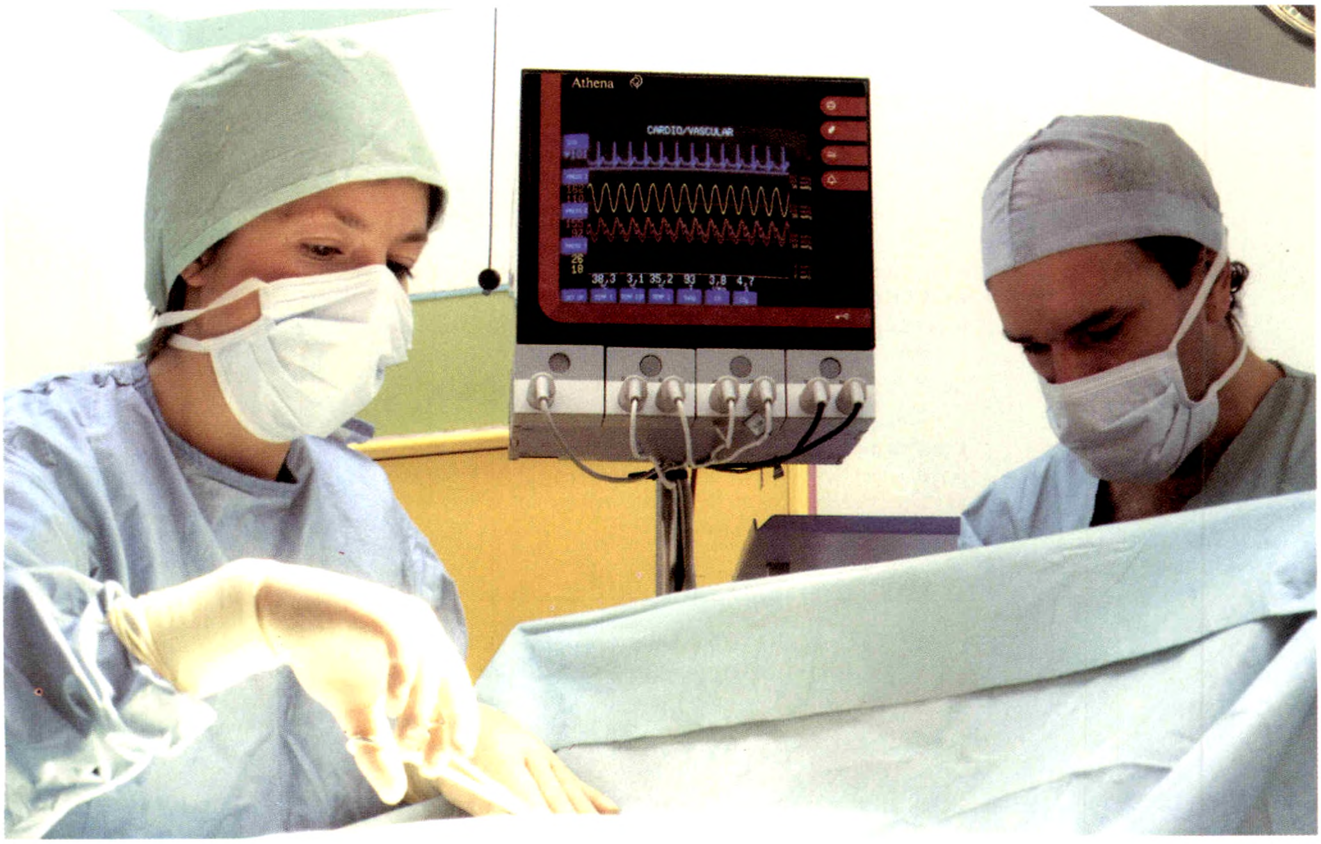

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not detected because of inadequate monitoring in the anaesthetic room?

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Wolff–Parkinson–White syndrome and ECG after operation

We report a case of Wolff–Parkinson–White (WPW) syndrome which highlights the potential for misdiagnosis of myocardial ischaemia. The syndrome is a form of congenital pre-excitation due to the presence of an accessory connexion between the atria and ventricles. This additional pathway is called the bundle of Kent. It is occasionally forgotten that this pathway may be interrupted; this causes the PR interval to revert to normal and produces a major change in the overall appearance of a twelve-lead ECG.

The patient was a 35-year-old woman admitted to hospital for a laparoscopic sterilisation. Her previous medical history was unremarkable with the exception of palpitations many years earlier, which was diagnosed as Wolff–Parkinson–White syndrome. She was taking no medication and was a nonsmoker. Examination was entirely normal and a pre-operative ECG confirmed type B WPW syndrome (Fig. 1a).

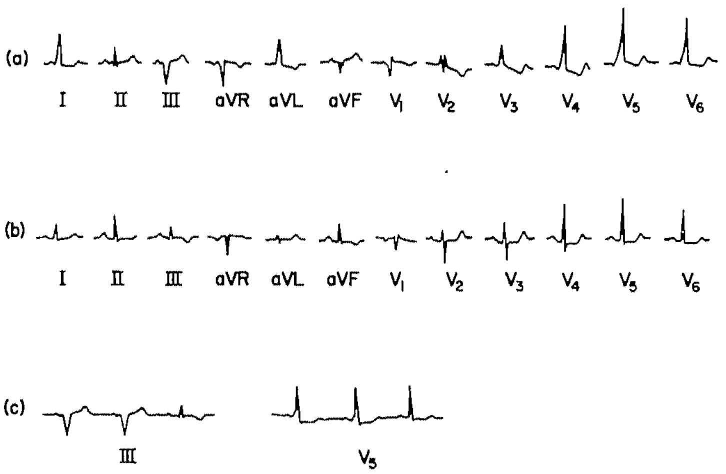

Fig. 1. (a) Pre-operative trace; (b) initial postoperative trace; (c) final trace showing normal and short PR intervals.

The patient was premedicated with temazepam 20 mg orally. ECG monitoring was started before induction of anaesthesia with fentanyl 100 μg, etomidate 20 mg and atracurium 30 mg. Anaesthesia, after tracheal intubation, was maintained with nitrous oxide 70% and enflurane 0.6–1%. No arrhythmia was noted throughout the operation. Residual relaxant was reversed with neostigmine 2.5 mg and glycopyrronium 0.5 mg at the end of the procedure. Recovery was unremarkable.

Six hours later the patient complained of mild retrosternal discomfort, and so a further ECG was requested. She did not complain of palpitations and her pulse was regular, with a rate of 80 beats/minute; the arterial blood pressure was 130/90 mmHg. The repeat ECG (Fig. 1b) showed several changes from the preoperative trace; the QRS complexes were now a normal shape with a normal PR interval, the T-wave was flattened in lead II and inverted in leads III and AvF and there was ST depression in leads V4–6.

The chest discomfort was thought to be the consequence of tracheal intubation but, on the basis of these changes, the possibility of acute myocardial ischaemia was considered. This was unlikely in view of her age, previous health and absence of predisposing factors, and so she was observed on the ward. An ECG taken the next day showed a mixture of normal and abnormal complexes exhibiting normal and short PR intervals (Fig. 1c). Her subsequent recovery was unremarkable and no elevation of cardiac enzymes was demonstrated.

The operative management of these patients is described.[1] The aim is to avert tachyarrhythmias by the avoidance of sympathetic stimulation, and this is probably best achieved by deep inhalational anaesthesia. This case demonstrates that problems may still occur after operation.

The PR interval may be altered by any anaesthetic agents which affects A-V conduction. Should this occur it can produce a major change in the appearance of not only the QRS complex, as is commonly described, but also in the ST segment and T-wave. This can mimic myocardial ischaemia or even infarction.

It is normally recommended that atropine be avoided in these patients due to the possibility of precipitating a tachyarrhythmia.[1] However, it is also recognised that it may produce a normal PR interval by the acceleration of the impulse transmission through the A-V node.[2] This effect, to our knowledge, has not previously been described with glycopyrronium, which we presume to be the causative agent. However, it persisted for longer than the normal duration of action of this drug.

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Absorption of buccal morphine

We were interested by the report from Fisher *et al.* (*Anaesthesia* 1988; **43:** 552–3) which compared the absorption of transbuccal morphine and oral controlled-release morphine. We were particularly interested by their suggestion that wetting the transbuccal tablet before administration may alter its absorption characteristics since we have investigated this point during a dose-ranging study of transbuccal morphine.[1]

Fourteen patients who were to have gynaecological, orthopaedic or general surgical procedures received a transbuccal tablet that contained 10 mg morphine (Napp Laboratories) 4 hours before the scheduled start of surgery. The tablet was administered dry to nine patients; for the other five, the tablet was moistened before placing it in the buccal sulcus. Venous blood samples were taken at 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10 and 12 hours after administration. The blood samples were collected into lithium heparin tubes, centrifuged at 3000 rpm for 15 minutes and the supernatant plasma separated and stored at −20°C until analysis.[2] Side effects of the drug or tablets were also noted.

There was no significant difference in the pharmacokinetic variables between the groups (Table 1); the time to maximum concentration tended to be longer in the wet tablet group, but this difference did not reach statistical significance. There was a high incidence of complaint about the bitter taste of the tablet in both groups.

Table 1. The pharmacokinetic variables of the absorption of morphine after transbuccal absorption from tablets administered dry or previously wetted. Values are shown as mean (SD).

	C_{max} (ng/ml)	AUC 0–12 (ng/ml hours)	t_{max} (hours)
Wet $n = 5$	2.12 (0.83)	9.34 (4.03)	6.9 (4.01)
Dry $n = 9$	2.0 (1.2)	8.59 (6.83)	4.0 (1.37)

C_{max}, maximum concentration of morphine; AUC, area under the plasma concentration time curve; t_{max}, time to reach maximum plasma concentration.

Plasma concentrations of morphine after transbuccal administration are reported as comparable to those after intramuscular administration.[3] However, more recent studies have demonstrated considerably lower plasma concentrations of morphine[4,5] and suggest that wetting the tablets before administration may be the cause of this difference. We found low plasma concentrations of morphine irrespective of whether the tablet was administered wet or dry. We suggest that this is due to poor transbuccal absorption of morphine and predominant enteral absorption, hence the bitter taste (as the tablets dissolve in saliva) and low bioavailability.

The difference in plasma morphine concentrations between centres may be as a result of different methods. The same pharmaceutical preparation was investigated in the previous studies[3–5] and plasma morphine concentrations in our study were comparable to those most recently reported.[4] Lack of resolution between morphine and morphine-6-glucuronide may overestimate morphine concentration by high performance liquid chromatography, if morphine-6-glucuronide is not available to calibrate the assay. This may be the cause of the higher values in the earlier study,[3] performed before morphine-6-glucuronide was widely available. Wetting the tablets before administration is unlikely to explain the difference in plasma concentrations of morphine between centres.

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A reply

Thank you for the opportunity to comment upon the interesting letter from Shelly and colleagues concerning the absorption of buccally administered morphine.

The plasma morphine concentrations measured in the course of their investigations are indeed comparable with those reported by ourselves and we note that they found no difference in the pharmacokinetic parameters C_{max} and AUC using wetted or dry buccal morphine tablets. We would point out, however, that Shelly and coworkers investigated a Napp Laboratories transbuccal morphine tablet, whilst we examined a Pharmax preparation. Unfortunately, we have no data on the pharmacokinetic effect, if any, of wetting the Pharmax buccal tablet before administration.

Our suggestion, that wetting the tablets before administration might alter the subsequent transbuccal absorption rate, was advanced as a possible reason for the disparity in morphine concentrations between our study using dry tablets and those of Bell *et al.*[1] who used wetted tablets of the same formulation. We pointed out that in spite of the fact that the analytical methods differ in our respective laboratories, we have measured similar morphine concentrations and time profiles after intramuscular morphine as have Bell *et al.* so that the differences between our respective results after buccal morphine administration seemed less likely to be due to assay methodology than to the possibility of altered absorption characteristics after wetting the tablet.

We are not convinced although it is possible that the suggestion that lack of resolution between morphine and morphine-6-glucuronide by high performance liquid chromatography (HPLC) caused the higher figures obtained by Bell *et al.* with buccal morphine tablets. Indeed, they stated in their paper that the method they employed[2] separates the parent drug from its glucuronide metabolites and we have shown, albeit with different HPLC conditions, the clear separation of morphine and morphine-6-glucuronide in our own laboratory using morphine-6-glucuronide to confirm peak identification. Were it the case that resolution between morphine and morphine-6-glucuronide was not achieved in the investigation of Bell *et al.* then, in order to explain our similar intramuscular results but dissimilar buccal results, it would also be necessary to postulate a different metabolic profile after the two routes with greater production of glucuronide after buccal administration.

This is a likelihood suggested both by the presence of glucuronidisation capacity in the buccal mucosa of various species[3] and by the possibility that buccal morphine absorption is predominantly enteral (as suggested by Shelly and colleagues in view of the high incidence of bitter taste reported in association with the tablet) and therefore subject to first-pass hepatic metabolism.

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Permanent record of findings at laryngoscopy

Difficult tracheal intubation still remains an important cause of morbidity and mortality in anaesthesia. It is a matter of concern to all anaesthetists and presents a challenge even for the most experienced clinician. An article or a letter relating to this subject has appeared in every issue of your journal this year.

The true incidence of difficult intubation is between 1.5–7% and depends on the surgical population assessed and the design of the study.[1,2] There have been numerous attempts to find a reliable predictor during assessment before operation to indicate the possibility of difficulty in intubation. The two most useful indicators seem to be: ability to visualise the soft palate (Mallampati's sign)[3] and testing extension of the head on the neck.[4]

The most obvious warning of an impending problem is the history of previously difficult intubation. One will usually find a note about the difficulty if the previous anaesthetic chart is available, with or without a description of the view seen at direct laryngoscopy. This is the most useful piece of information as far as the future management is concerned.

Cormack and Lehane[5] classified difficult intubation into four grades, according to the view obtained at laryngoscopy. Grade I, most of the glottis visible; grade II, only epiglottis and posterior commissure visible; grade III, no part of the glottis can be seen but only the epiglottis; and grade IV, not even the epiglottis can be exposed. The accompanying Figure in their original article of all four views very accurately reflects the true-to-life situation.

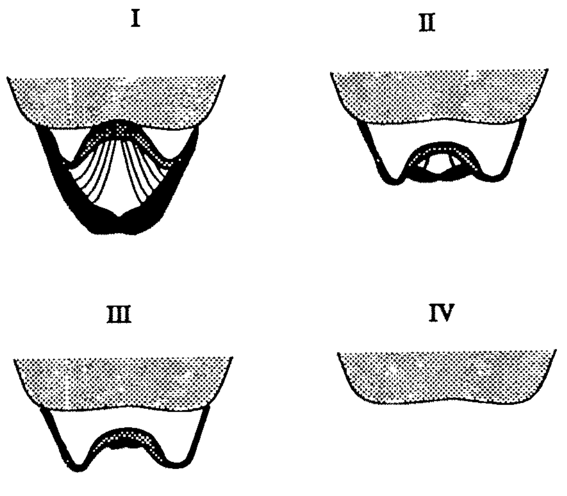

Fig. 1. Diagrammatic interpretation of four grades of laryngoscopy as described by Cormack and Lehane.[5]

A similar figure should be adopted in diagrammatic form (Fig. 1), and be present on the anaesthetic sheet so that after each laryngoscopy one can tick or encircle the appropriate view. This would serve as the best guide for the anaesthetist involved in future operations and also establish some uniformity within the profession, as far as classification of difficult intubation is concerned.

All newly designed anaesthetic charts should I propose, have the above Figure of four grades of laryngoscopy incorporated in their design. A medical equipment company has offered to manufacture a rubber stamp with the Figure described above, free of charge.

This proposal had the overwhelming support from 90 participants, (72 consultants) who came from every part of the country at a meeting recently.

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Tracheostomy in obstetric practice?

The extremely difficult intubation, as described in a patient with infertility by Callander and Thomas (*Anaesthesia* 1988; **43:** 703–4), does indeed raise many problems, but to suggest to elective tracheostomy in late pregnancy with its accompanying psychological trauma and possible morbidity, appears horrendous. Surely, the answer to the airway problem lies in regional block, either epidural or spinal, and the avoidance of general anaesthesia?

We found, before the widespread introduction of epidural block for Caesarean section, that in about 1% patients for Caesarean section the trachea could not be intubated. These patients, six or seven each year were informed of their airway problem and given an explanatory letter which recommended regional block for any future surgical intervention. None of these patients developed either ectopic pregnancy or antepartum haemorrhage (which worried the authors with their patient) but we have successfully managed such cases under epidural block on numerous occasions.

Marked hypotension would be an obvious contraindication to regional block, but early diagnosis and treatment can usually avoid this problem. For instance, whilst the incidence of ectopic pregnancy is increased after tubal surgery, early laparoscopic and ultrasonic diagnosis followed by surgery can greatly reduce the occurrence of the dramatic 'ruptured ectopic'. Laparoscopy in a patient whose trachea cannot be intubated may be performed under epidural or spinal block, although pain referred to the shoulder may be a problem if the abdomen is over distended with the gas for insufflation. Anaesthesia for laparoscopy with a facemask and spontaneous ventilation seems to be gaining popularity in clinical practice and may be considered another alternative to intubation. One advantage of a regional technique is the ability to administer 100% oxygen under epidural or spinal block, without unplanned awareness.

It is difficult to understand why the patient was subjected to 1 hour and 50 minutes of attempted awake intubation when her trachea was reported to be nonintubatable on two preceding occasions, and the operation could have been easily undertaken under epidural or spinal block, with (or without) sedation.

The letter discusses 'an unusual dilemma of ethics related to anaesthetic practice'. Surely, in this case, no dilemma should exist, and regional block be offered on each occasion, not tracheostomy.

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Adrenaline and anaphylaxis

Recent reports (*Anaesthesia* 1988; **43:** 953–61) highlight an apparent reluctance of anaesthetists to use adrenaline for the initial treatment of anaphylactoid reactions.

Hydrocortisone was the first drug given to these cases and adrenaline only later, in two cases after cardiac arrest had already occurred. Hydrocortisone may have a role in the management of persistent bronchospasm, but has an onset of action measured in hours and does not relax bronchial smooth muscle, inhibit mediator release from mast cells or antagonise histamine at receptor sites.[1] It therefore seems to have little place in the acute stages of anaphylactoid reactions when prompt and specific treatment are essential. Adrenaline continues to be the recognised first-line drug treatment of such reactions[1–3] and a 1 in 10 000 solution should be given intravenously in 1-ml increments.[4]

Anaesthetists are understandably cautious about using adrenaline during anaesthesia, but we should recognise its early and specific role in life-threatening cases of bronchospasm and hypotension due to anaphylactoid reactions.

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A reply

We are grateful to Dr M. Parsloe for stating so positively the need for immediate administration of adrenaline to patients with anaphylactic or anaphylactoid reactions. Discussion and comments on treatment were not within the scope of our published article (*Anaesthesia* 1988; **43:** 958–61), which leant towards the possibility of prophylactic testing. In the three reported cases (*Anaesthesia* 1988; **43:** 953–61) adrenaline was given. The apparent reluctance of anaesthetists to use adrenaline early in our case may be because of two factors.

Uncertainty of diagnosis, at least at first, in an otherwise healthy patient with no history of allergy, who was given a general anaesthetic for the first time. Her blood pressure and ECG were monitored. The initial bronchospasm was only momentary. She had no other features that would suggest an anaphylactic or anaphylactoid reaction.

Presence of gross tachycardia in a case where the diagnosis is uncertain. Initially, the BP and cardiac monitors showed a systolic pressure of 110 mmHg and a sinus tachycardia. Time was spent in the establishment of an airway, oxygenation and an intravenous infusion; though the latter was given. Gross hypotension and respiratory arrest occurred and the cardiac rate plummetted rapidly to 12 beats/minute, so a cardiac resuscitation procedure was adopted, and intravenous atropine and 1 in 10 000 adrenaline were given, with immediate restoration of a tachycardia, a systolic pressure of 80 mmHg and spontaneous ventilation.

We agree that adrenaline is the first-line drug for treatment of anaphylactic or anaphylactoid reactions. Not only does it counteract the response to the released pharmacological mediators (via α and β-adrenoceptors), but it also inhibits the release of those mediators (an action via β-adrenoceptors)[1] if given early enough, ideally at the time of triggering of reaction.

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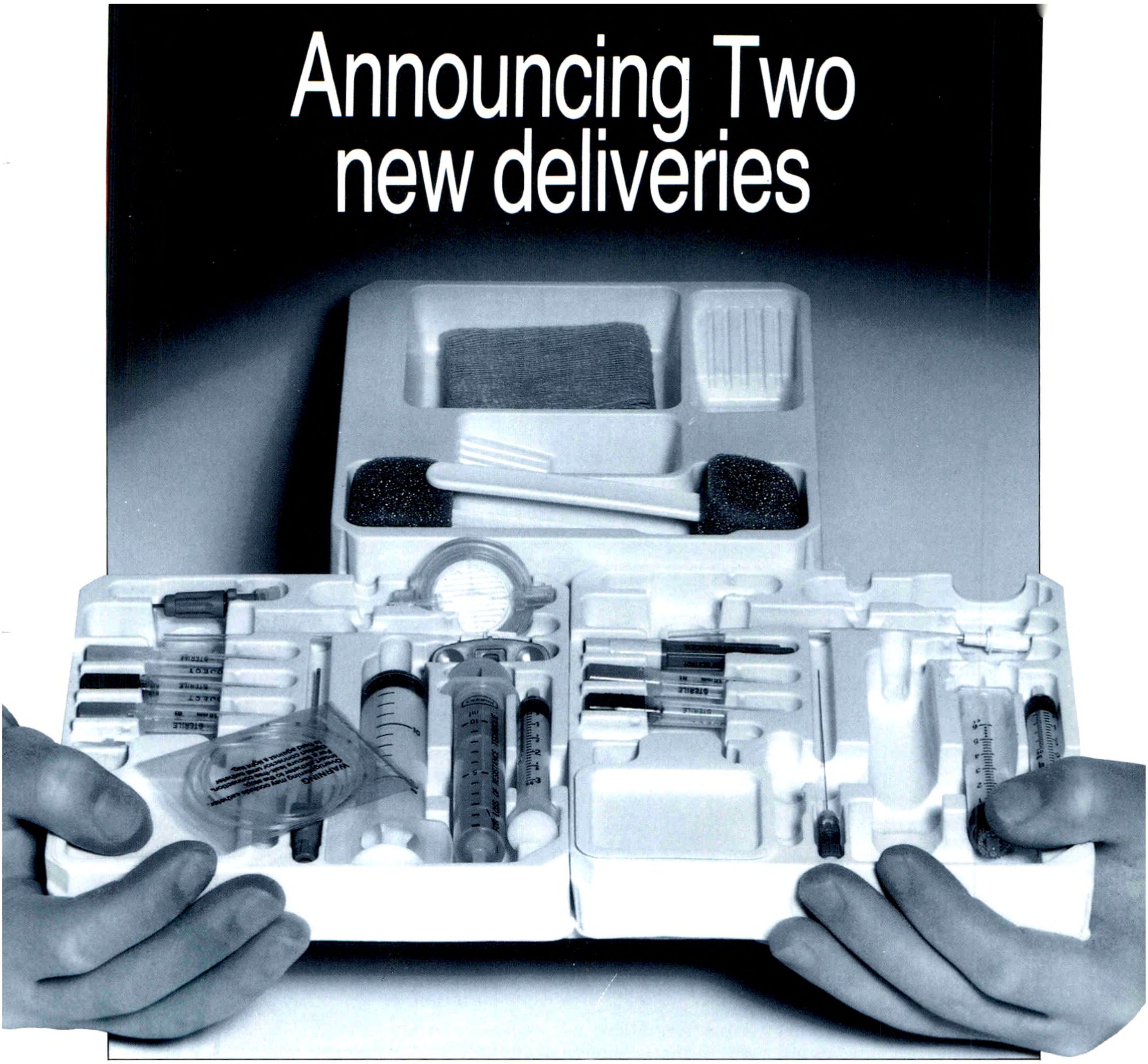

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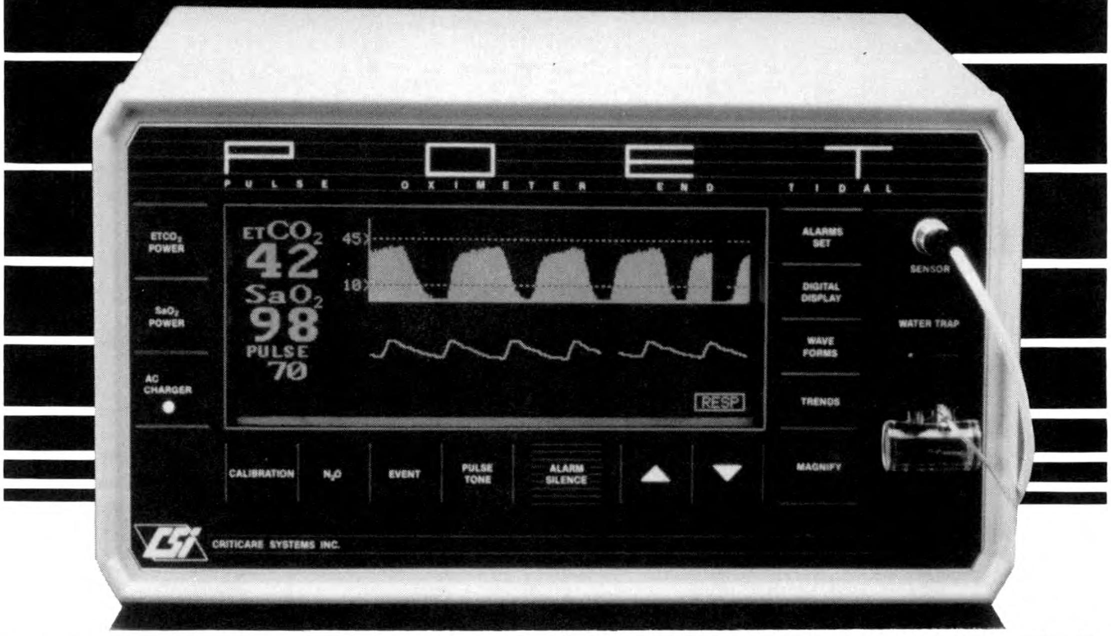

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A reply

Thank you for the opportunity to reply to the letter from Dr M. Parsloe. His views on the life-saving role of adrenaline in anaphylactoid reactions are of course correct but there were two reasons why there was delay in its administration.

The patient was asthmatic and had a history of pneumothoraces. There were many more likely causes of our failure to ventilate her lungs than anaphylaxis and these were considered in turn. Adrenaline was soon given once the wheals were noted and a diagnosis was established.

Hydrocortisone was given first merely because a ready prepared syringe was available. We had intended to give this during anaesthesia.

Our paper was a case report and we did not advocate that our treatment was that of choice.

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E.J. Fazackerley

A reply

We agree with Dr Parsloe about the importance of adrenaline in the management of anaphylactic reactions.

Our patient was treated with adrenaline and corticosteroids almost simultaneously, but we are sure that her quick and good recovery was undoubtedly as a result of the administration of adrenalin.

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Defibrillator failure in a magnetic resonance unit

A magnetic resonance (MR) imaging and spectroscopy system using a 2 teslar magnet, has been operational in Liverpool University for over a year.

A variety of problems with monitoring and other equipment have arisen, including the failure of a Simonsen and Weil DMS 930 defibrillator. The magnetic resonance unit, whilst fitted with radiofrequency screening, does not have an effective magnetic field screening. The failure of the defibrillator occured in an anaesthetic/recovery room, adjacent to the scan room. It was thought to be at a safe distance from the main source magnetic field, although there is a field drop across the room from 50 to 10 gauss.

The DMS 930 defibrillator was chosen because a lightweight, detachable, LCD ECG monitor was included. The latter proved to function within the scan room where no standard CRT display would operate. It was found to 'switch off,' however, when placed within 2 m of the imaging coil. The defibrillator itself was not taken within the scan room since it contained substantial items of magnetic material. It suddenly failed after a month of normal function and was replaced by another unit. This second unit also failed routine testing some 3 weeks after its introduction; it was also kept in the 'safe area' of the anaesthetic/recovery room. It appeared to recover its normal function on removal from the magnetic resonance unit building for 10 minutes, only to fail an hour or so after its return to the anaesthetic room. This process was repeated several times and strongly suggests a link between the environment of a substantial magnetic field and the failure of the defibrillator.

Electromechanical equipment may contain a variety of items which can be affected by a strong magnetic field (relays, ferrite tuning coils etc.). The example described here shows that equipment failure may not be immediately evident after its introduction into the MR environment and demonstrates the need for frequent tests of any potentially susceptible equipment in such situations. It also emphasises the need for effective magnetic field screening in MR units.

The failure of a variety of equipment in areas, thought originally to be at a safe distance, is now causing substantial problems in providing suitable monitoring and resuscitation equipment within this MR unit.

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Unusual tracheal tube obstruction leading to an unusual bronchoscopic technique

A problem was encountered with a Brandt, Hi-Lo Mallinckrodt tracheal tube with a Murphy tip. A 44-year-old man who was to undergo elective aortic valve replacement was noted to have a short, immobile neck, receding mandible and prominent upper incisors. Tracheal intubation with a size 9 Brandt Mallinckrodt tracheal tube was difficult, the epiglottis could be viewed but the cords could not (Grade III of Cormack and Lehane).[1] The tracheal tube was inserted blind over a gum elastic bougie and was noted to be correctly placed. Ventilation of the lungs was continued in the postoperative period without any apparent problem. However, after 9 hours it was found that suction catheters, which had till then functioned normally, would not pass beyond the end of the tracheal tube. There was evidence of accumulated secretions on auscultation and a chest X ray confirmed the clinical impression of bilateral basal collapse. The tip of the tracheal tube was above the carina. Blood gases demonstrated a progressive deterioration in ventilation. The patient was sedated with 5 mg of midazolam, paralysed with 10 mg of vecuronium and an Olympus wide bore (5.9 mm diameter) fibre optic bronchoscope was passed down the tracheal tube. The distal port of the tracheal tube was found to be closely applied to the anterolateral wall of the trachea and neither bronchoscope nor a gum elastic bougie would pass beyond it. The Murphy's eye was close to, but not touching, the tracheal wall and allowed ventilation with no increased ventilatory pressures or chest hyperinflation, though suction was impossible. The bronchoscope was passed alongside it through the mouth, in view of the previous difficult intubation and the hypoxia secondary to accumulated secretions and collapse before changing the tracheal tube. This allowed suction to the oropharynx and main airways under direct vision, and with 'bagging' produced an improvement in the oxygen saturation recorded on a pulse oximeter. The bronchoscope was resited in the trachea with a second tracheal tube passed over it. The old tube was removed and the new one advanced, but it required the use of a Macintosh laryngoscope to manoeuvre it past the epiglottis.

It is interesting to note that the distal port of a Brandt Mallinckrodt tube should be occluded by the wall of the trachea, since at body temperature it is supposed to alter shape to conform to the anatomy of the patient, and should not occlude. However, it appears that some aspect of the patient's anatomy distorted the tube so that the end hole became obstructed.

Another point of interest in this case was that the fibre-optic bronchoscope could be passed successfully alongside the blocked tracheal tube, to allow suction and general improvement in the patient's condition before a difficult change of tube was undertaken. The difficult re-intubation in this case may have been compounded by using the oral approach[2,3], which was prompted by following the first tube with the bronchoscope.

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'Trial by Ordeal' by the Calabar (physostigmine) bean

It was fascinating to read the interesting historical article by R.W.D. and E.A. Nickalls. They reproduce and comment upon a translation of Dr Kleinwachter's 1964 article on the use of physostigmine (eserine) solution derived from the 'Calabar' (or West African) 'Ordeal' bean (*Anaesthesia* 1988; **43:** 776–9).

May I be permitted to draw attention to previous references to trial by ordeal with the Calabar bean which appeared in *Anaesthesia* in 1979 (**34:** 104–5 and 226) in the ingenious quiz series originated by Dr W.B. Clarkson of the Royal Devon and Exeter Hospital? An illustration (*Anaesthesia* 1979; **34:** 105) shows the explorer Richard Lander ('discovery of the mouth of the Niger') about to undergo trial by ordeal in 1827 by drinking a 'bitter water' solution prepared from Calabar beans. Lander survived his 'trial', much to the surprise of the onlookers and was subsequently treated almost as a god. His survival was put down by others to 'strength of constitution or connivance of the fetish-man (witch doctor), or for some other occult reason'.[1]

Lander's trial by ordeal took place 28 years before Christison's paper on the 'Ordeal-bean of Old Calabar, Western Africa,[2] to which Nickalls and Nickalls refer, but is it possible that Lander, or the fetish-man, were aware of the mutual antagonism of extracts of the Calabar bean (*Physostigma venenosum*) and the leaves of deadly nightshade (*Atropa belladonna*) or a similar plant?

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Honorary Archivist

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Extradural fentanyl and dystrophia myotonica

This is a report of an approach to the management of postoperative pain in a patient with dystrophia myotonica (DM).

A 61-year-old man who weighed 60 kg was prepared for iliofemoral and femorofemoral bypass grafting. Generalised muscular weakness was confirmed and grip myotonia was elicited. The patient's ECG showed first degree heart block. Chest X ray showed an enlarged heart, and lung spirometry demonstrated a mild restrictive ventilatory defect.

Premedication was with temazepam 10 mg orally. ECG and blood pressure (BP) were monitored noninvasively on arrival in the anaesthetic room and a 16-gauge cannula was placed in the arm. Compound sodium lactate 500 ml was given as a preload.

An extradural catheter was inserted into the T_{7-8} interspace and increments of 0.5% plain bupivacaine to a total of 11 ml were injected extradurally. The systolic blood pressure decreased to 80 mmHg. Dextrose 4%/saline 0.18% 500 ml and methoxamine 8 mg in two divided doses were given intravenously to increase the BP. Analgesia was achieved from T_2 to T_{12} dermatomes bilaterally using a pinprick test.

Induction and maintenance of anaesthesia was then accomplished by halothane 0.5–1% and nitrous oxide 60% in oxygen, using a facemask and a Lack breathing system, and the left radial artery was cannulated.

The patient's breathing became laboured after 2 hours. Vecuronium 2 mg was then given to facilitate tracheal intubation and intermittent positive pressure ventilation of the lungs was started to maintain an end-tidal CO_2 of between 4.5 and 5%; the surgical procedure lasted 4.5 hours.

A bolus of 50 µg fentanyl (concentration of 5 µg/ml) was given extradurally 15 minutes before the end of anaesthesia. The patient awakened promptly at the end of surgery, and showed good muscle power by coughing on the tracheal tube and by an adequate inspiratory volume. The muscle paralysis was not reversed; the trachea was extubated, the patient transferred to the intensive care unit, and a continuous extradural infusion of fentanyl was started at a rate of 10 ml/hour, of the same concentration as before. There were three brief self-limiting episodes of severe bradycardia (20–30 beats/minute), and the patient remained comfortable and pain free on this analgesic regimen, which varied between 10–12 ml/hour. He was then returned to the general surgical ward after 4 days and discharged home 21 days after operation.

Muscle wasting and weakness in DM may cause hypoventilation, marked somnolence and grossly irregular patterns of breathing. A defective medullary respiratory control has been proposed to be responsible for these abnormalities.[1] The administration of opioids to DM patients have been implicated as causes of inability to maintain an airway, hypoventilation, apnoea and cardiovascular catastrophes.[2]

Extradural fentanyl was shown to provide better pain relief and have less systemic side effects in comparison to conventional intramuscular opioids.[3] A concentration of 10 μg/ml was optimal for pain relief, but the dilute form of 5 μg/ml was associated with few side effects such as sedation, nausea and vomiting.[4]

The usual causes of death in DM are respiratory failure, bronchopneumonia or cardiovascular abnormalities that progress to heart failure or complete heart block.[5] This led us to refer the patient to a cardiologist, especially after several episodes of perioperative bradycardia.

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The epidural space

Dr Blomberg's article on the paramedian approach to the epidural space (*Anaesthesia* 1988; **43:** 837–43) is further evidence of the determination of anaesthetists to discover what happens when a needle is inserted into the epidural region. It is unfortunate that this cannot be done without breaching the integrity thereof.

Endoscopy has been used increasingly to examine the interior of naturally occurring cavities, and this burgeons the caveat that there is no naturally occurring cavity between the dura mater and the contents of the epidural region.[1,2] The insertion of a Tuohy needle displaces the dura away from the walls of the vertebral canal and creates an epidural space. This displacement is compounded by the insertion of the epiduroscope; the anatomy is distorted because the dura is not supported by the presence of cerebrospinal fluid pressure in the cadaver.[3] This artefact would be lessened, but not removed if the subarachnoid space were filled with fluid through a cisternal puncture before the insertion of the needles.

The presence (or otherwise) of a dorsomedian connective tissue band is also a recurrent theme. What is described is probably the result of displacement of the posterior deposit of fat, which is situated in the area between the ligamentum flavum and the dura mater, rather than the existence of a dorsomedian fold of dura mater as described elsewhere.[4,5] This deposit of fat may be displaced either by the tip of the Tuohy needle as it is inserted into the epidural region, or by the injection of fluid through the needle. It may also be displaced as a secondary response to the displacement of the dura mater, to which it is attached, as is shown clearly in the epiduroscopy photographs of Dr Blomberg.

It is interesting to examine the paramedian technique employed by Dr Blomberg, since it appears to be rather different from that described in British texts,[6] and the one I use myself, in which the needle angle to the dorsal plane is rarely greater than 100°. This latter technique has the disadvantage of approaching the dura at the normal, unlike the more obtuse, approach which has the advantages described.

Inevitably the only way in which a true comparison between midline and paramedian approaches can be made is to examine them in the clinical situation and see whether there are obvious differences in the incidences of dural taps, unilateral blocks, and incomplete blocks, which are the ultimate arbiters of epidural technique. Until then we can always hope that the advancement of noninvasive imaging techniques may be employed to assist us in a greater understanding of the epidural region by examining it in its intact state.

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A reply

Dr Harrison has kindly commented on my article and I am grateful for the opportunity to make this reply.

Dr Harrison points out the following factors on which we fully agree, which I hope is evident from the present paper as well as my previous ones on endoscopy of the epidural space.

Endoscopy may cause artefacts of the structures of the epidural space and their relationships. This disturbance must, however, be less than that of other current methods for investigation of the space, with the exception of such radiological methods as computerised tomography.

Conclusions derived from examination of cadavers to the clinical situation must be made with great care and only clinical studies can definitely decide the advantages or disadvantages of any technique. However, epiduroscopy has made it possible to demonstrate technical aspects of the two techniques in the same autopsy subject in a way that has not been possible before.

Finally, the absence of cerebrospinal fluid (CSF) pressure and circulation in the cadaver makes the direct transfer to the clinical situation of distances measured in cadavers not justifiable.

There appear to be some difference of opinion about the existence of the dorsomedian connective tissue band. A variation in appearance was demonstrated (reference 4 above); each band consisted of strands of connective tissue (with the exception of two which presented with a complete membrane) which attached the dura to the dorsal aspect of the epidural space in a manner that fat alone possibly could not do. This attachment caused a dorsomedian fold of the dura mater which was accentuated by the introduction of the endoscope, needle and catheter (and, of course, by the very low or absent CSF pressure and absent circulation). These attachments of the dura to the dorsal aspect of the space were so strong in some cases, that at the end of the examination a forceful push of the endoscope against the dura mater was necessary in order to break them up. Such behaviour would not be expected if only fatty tissue were concerned.

This appearance of the band has constantly recurred in epiduroscopic examinations in more than 30 cadavers as well as in 10 patients.[1] The epidural space *in vivo*, also presented mainly as a potential space, as suggested by Dr Harrison.

Support for the dorsomedian connective tissue band is given in a recent study of the epidural space with computerised tomography by Savolaine *et al.*[2] They verified the structure although they called it the 'plica mediana dorsalis'; this is a term which, in my opinion, should be reserved to identify the fold in the dura mater that is caused by the connective tissue band. It, together with laterally extending connective tissue bands, divided the epidural space into potential compartments.

A clinical study has just been completed in 50 patients subjected to transurethral resection of the prostate or resection of a bladder neoplasm with epidural analgesia, to compare the midline and paramedian approaches. The results of this study are now being analysed and will be presented in the near future.

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Shivering and epidural blockade

Drs Matthews and Corser (*Anaesthesia* 1988; **43:** 783–5) describe the use of epidural fentanyl to promote cessation of shivering over a 15-minute period. They do not state the proportion of patients in whom the epidural was being given for obstetric analgesia, but in my experience it is unusual for shivering to be sufficiently marked or prolonged to cause distress in such parturients. Epidural block for elective Caesarean section does indeed frequently cause uncomfortable and embarrasing shivering. It also increases oxygen consumption.

Walmsley *et al.*[1] have described the temperature changes within the epidural space after epidural injection of chilled and warmed bupivacaine; cessation of shivering produced by the latter corresponded well with the period in which epidural temperature increased. The triggering of shivering after epidural blockade appears to involve thermoreceptors in the spinal cord. Some individuals are probably more susceptible than others, since only 47% shivering occurred after epidural injection of bupivacaine at 4°C. Ponte *et al.*[2] recommended warming of the injectate to minimise shivering.

We have found in contrast to Drs Matthews and Corser that warming the bupivacaine ampoules and syringes before administration has reduced the incidence of shivering dramatically; indeed those shivering beforehand stop shivering after the epidural. The ampoules and syringes are placed in the warming cupboard the evening before. Astra Pharmaceuticals report that their products are stable at 37°C for at least one month. Shivering, since the adoption of this simple manoeuvre, has been seen in 6% in a personal series, is never marked or prolonged although sometimes begins in the recovery ward, and the author uses warmed saline to terminate shivering at this stage.

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The study by Dr Matthews *et al.* (*Anaesthesia* 1988; **43:** 783–5) was interesting. In his discussion Dr Matthews states that the cause of shaking after epidurals is still unknown and lists some theories. The scientific world may no longer ponder this question but perhaps the time is ripe to share my misconception/inspiration.

Local anaesthetics when introduced into the epidural space cause blockade of the sympathetic supply to a portion of the body. Blood then starts to pool in this portion while those parts not blocked experience profound sympathetic stimulation to compensate. The sympathetic activity diverts blood away from the skin which exhibits piloerection. The reduced skin blood flow in the unblocked segment of the body causes this skin to cool and so stimulates the cutaneous thermoreceptors which in turn activate the hypothalamic temperature-regulating centres and shaking or shivering ensues. Indeed if one observes patients shortly after the injection of local anaesthetic into the epidural space one regularly sees a clear demarcation line of goose-pimples at the upper reaches of the block, especially in those patients who shake.

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B.C. O'Sullivan

A reply

Thank you for the opportunity to respond to the letters from Drs O'Sullivan and Mackenzie.

The hypothesis expounded by Dr O'Sullivan, whilst superficially attractive, does not explain the virtual absence of shaking associated with the intrathecal administration of bupivacaine, where compensatory sympathetic activity also occurs. Furthermore, shaking associated with epidural anaesthesia begins within 10 minutes in 75% of mothers, before a substantive sympathetic block has developed.

It is indeed unusual as Dr Mackenzie states, for shivering to cause distress. Our study took over one year to complete and contained 44 patients (out of a total of 50) in whom the epidural was inserted for analgesia in labour. Two thousand four hundred epidurals are performed per year and so the incidence of shaking severe enough to cause distress is less than 2%. However, particularly in this healthy population, any complication is important.

Two well controlled clinical trials[1,2] have shown no correlation between injectate temperature and shaking. Another study[3] used a thermal shock of bupivacaine at 4°C, compared to bupivacaine at 37°C and found that two patients in the warm group, compared to nine patients in the cold group shook; this is a statistically significant difference.

The other study, quoted by Walmsley *et al.*[4] also used bupivacaine at 4°C. Fourteen out of 30 patients shook, an incidence equivalent to that seen after the injection of bupivacaine at room temperature.[5] The onset of shaking did not correlate with the lowest epidural temperature. Eight patients had significant shaking, and four responded to the injection of bupivacaine warmed to 41°C, though in these four the cessation of shaking correlated with the increase in epidural temperature.

Thermosensitive tissue almost certainly exists within the spinal cord, though shaking is a multifactorial phenomenon. The natural incidence of shaking (without intervention) is 10% during the first stage and 20% thereafter,[6] somewhat higher than that seen by Dr Mackenzie. Personal series stimulate controlled clinical trials.

The evidence regarding injectate temperature is equivocal as originally stated.

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DDAVP and open heart surgery

The recent report (*Anaesthesia* 1988; **43:** 898) of the use of [1-deamino, 8-D-arginine] vasopressin (DDAVP) in a patient with Type 1 von Willebrand's disease and reference in the report to its use in haemophilia A prompts us to draw attention to the use of DDAVP to reduce bleeding after cardiac surgery.

Factor VIII:von Willebrand factor (vWF) is necessary for the adhesion of platelets to subendothelial connective tissue and thus has a vital role in the formation of the platelet plug. DDAVP increases plasma concentrations and activity of vWF. It shortens the bleeding time in normal individuals as well as those with von Willebrand's disease.[1]

Bleeding after cardiopulmonary bypass (CPB) is due to many factors but an acute acquired defect of platelet function is considered most important.[2,3] The degree of impaired platelet function is proportional to the duration of CPB and probably also to the level of hypothermia.[2] vWF is adsorbed on to nonbiological surfaces and levels may be reduced by passage through the oxygenator apparatus.[4] vWF is required for ristocetin-induced platelet aggregation and the observed defect in ristocetin-induced platelet aggregation after protamine administration to patients after the termination of CPB, suggests that reduced levels of vWF are contributory to the haemostatic defect of such patients.[5]

Levels of vWF can be increased exogenously by the administration of cryoprecipitate or endogenously by giving DDAVP. Mean operative and early postoperative blood loss was significantly reduced (by up to 40%) in a controlled trial of 70 patients who had various cardiac operations that required CPB (excluding coronary artery bypass grafting), among the patients who received 0.3 μg/kg DDAVP after the termination of CPB and after the administration of protamine. The haemostatic role of vWF was further supported by the observation that patients who suffered the greatest blood loss had relatively low preoperative levels of vWF.[6] No side effects of DDAVP were noticed in this study; in particular there was neither antidiuretic effect nor any increased incidence of thrombosis. However, until further studies are performed, it would be prudent to avoid the use of DDAVP in uncomplicated coronary bypass surgery in view of the possibility of graft occlusion.

Dramatic reductions in peri-operative blood loss have also been acheived using aprotonin, an inhibitor of trypsin, plasmin and kallikrein. Aprotonin, when given by loading dose before sternotomy followed by an infusion, reduced postoperative drainage loss by 81% and reduced the need for transfusion.[7] But the total cost of the recommended 5×10^6 KIU (kallikrein inactivating units) is £162.00 compared with £5.35 for 20 μg DDAVP, so that until a controlled trial that compares the two drugs is available, the use of DDAVP in selected cases seems more appropriate.

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Ketamine–midazolam continuous infusion in cardiac surgical patients

We have studied 20 ASA class 3–4 patients during aortocoronary bypass graft and (or) valvular replacement surgery. Seventy percent of the patients had ejection fractions less than 0.4. Ten patients were given ketamine–midazolam continuous infusion, and 10 patients received high dose fentanyl (75 μg/kg) as control. All patients were premedicated with lorazepam 2–4 mg by mouth one hour before surgery. Five lead ECG, arterial lines, pulse oximetry and pulmonary arterial pressures were monitored routinely. Ketamine 2–10 mg/kg/hour and midazolam 0.1–0.5 mg/kg/hour were the only anaesthetic agents used from the beginning of the case until cardiopulmonary bypass was started. In the control group, 75 μg/kg of fentanyl was given over 3–5 minutes at the time of the induction and no other anaesthetic agent was then given. The lungs of both groups of patients were ventilated with 100% oxygen.

Our results show that none of the patients in the ketamine–midazolam group had statistically significant changes in blood pressure or heart rate during induction, tracheal intubation, skin incision or sternotomy ($p > 0.05$). The control group showed statistically significant changes in blood and heart rate during induction, tracheal intubation and skin incision ($p < 0.05$). None of the patients in either group had any recall of surgery or psychotomimetic reactions postoperatively nor did they have S-T segment changes intra-operatively.

This study suggests that a ketamine–midazolam continuous infusion is associated with excellent haemodynamic stability and would be a good choice in cardiac surgical patients, especially those with poor left ventricular function.

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Abreaction on recovery from propofol anaesthesia

The study by Drs Miller and Jewkes (*Anaesthesia* 1988; **43:** 738–43) provided further evidence of the superior recovery from propofol-based anaesthesia in patients who undergo daycase surgery.[1–3] Until recently, I would have completely shared their enthusiasm.

A 24-year-old 82.5 kg woman who was to have cervical coagulation as a daycase in the early afternoon, agreed beforehand not to have drug premedication to facilitate her early discharge. She was calm when seen on the ward, but she became extremely agitated by the time she presented for anaesthesia. She revealed during a conversation with a nurse about the reasons for pre-operative starvation that she had consumed some chocolate 8 hours earlier, previously denied. She could not be wholly convinced that she was not at risk despite repeated reassurances. The urgency of her surgery precluded cancellation, and anaesthesia was induced with 0.1 mg fentanyl and propofol 160 mg, and maintained with 66% nitrous oxide and oxygen and a further 20-mg bolus of propofol. Spontaneous arm movement occurred within 30 seconds of the end of surgery and she began to moan loudly. She immediately opened her eyes when her name was called, and began shouting phrases such as 'not him', 'it's not the dog's fault' and 'don't kill Porky'. Attempts to restrain and calm only precipitated further outbursts, and the patient was sedated with 2 mg midazolam to prevent self-injury. She was fully orientated when she recovered 10 minutes later and showed no repetition of the previous behaviour. Questioned later before discharge, she had no recollection of the abreaction but was able to identify each phrase with a traumatic event from her childhood on a farm, mostly associated with the deaths of favourite animals. This incident has been reported to the Committee on Safety of Medicines for consideration as a suspected adverse reaction associated with anaesthesia.

It has become my practice in similar situations to sedate very nervous unpremedicated patients with 20–40 mg propofol given 1–2 minutes before induction. It is usually then possible to reduce the induction dose of propofol by a similar amount; the patients recover more peacefully as a result.

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A reply

Hallucinations, both pleasant and unpleasant, after propofol are widely reported.

In this case, albeit after a generous dose of fentanyl, only 2.18 mg/kg was given for both induction and maintenance. The recommended induction dose is 2–2.5 mg/kg; the length of the procedure is not given. The induction dose in our study was 2.5 mg/kg in unpremedicated patients after alfentanil 500 μg; maintenance dose was 0.3 mg/kg/minute that is 24.75 mg/minute for an 82.5 kg patient. Unduly nervous patients in my clinical experience may require 30–50 mg more than the predicted induction dose.

Light anaesthesia should be considered as a cause for this patient's reaction to propofol. Most dreams and hallucinations associated with propofol are enjoyable—my patients seem to dream most about holidays if they do dream.

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J.M. MILLER

Normal chest expansion with oesophageal placement of a tracheal tube

This is a report of a recent observation in a slender teenager whose oesophagus was intubated, and in whom chest movement appeared to show normal inflation without alteration in these movements when the tube was subsequently placed in the trachea.

A 13-year-old fit slender female presented for tonsillectomy. The trainee operating department assistant passed a 7.5-mm cuffed oral tube which seemed to pass without hindrance. The cuff was inflated with only 2 ml air to produce a seal, and inflation of the chest continued with a T-piece system and 500 ml bag. Chest expansion appeared normal, particularly in the upper part of the chest, which was exposed to observe the expansion. This movement and the low-volume cuff seal reassured all present that the tube was correctly placed, but my normal practice now is to confirm correct placement with tactile tests,[1] and the test was negative. Repeat laryngoscopy not only confirmed the oesophageal misplacement, but also showed that the tube was a snug fit in the region of the cricopharyngeus muscle. The larynx could not be intubated with this size of tube though size 7.0 mm proved suitable and was placed under direct vision. There was no difference between chest movements with correct placement and the earlier movements.

It might be argued that the tube was originally immediately above the cords and then displaced into the oesophagus but there are a number of reasons to discount this. Firstly, the tube was too large for the patient and could not be put in this position when we tried again. Secondly, we attempted inflation of the lungs during the tactile tests and subsequent laryngoscopy and there was no change in the chest movements. Finally, it seems most improbable that an airtight seal could be made so easily if the cuff was high in the pharynx.

Pollard and Junius described four cases in whom chest movement was considered to be a misleading sign.[2] One of these patients was slender. This was particularly misleading because this was one of the few reported cases in which irreversible brain damage occurred in a previously fit individual attended by a a specialist anaesthetist. Pollard and Junius suggested that inflation of the oesophagus alone might account for these observations and, although in our patient observation of the epigastrium was limited at first, there was certainly no progressive distension of the stomach with time.

It is likely that both ends of this viscus would need to be sealed if the oesophagus is inflated under these circumstances. That seems to imply that an easy seal with the cuff would almost be a necessary condition for it to happen. In effect two apparently different signs to confirm intubation act together to produce an even more misleading picture. It is worthy of repeated emphasis that even slender patients may have chest movement which exactly mimics that after tracheal intubation when the tube is misplaced.

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Flumazenil infusion or repeated doses

We were not offered the opportunity to reply to Dr R. Telford's letter (*Anaesthesia* 1988; **43:** 901) before its publication, in which he comments on our case report which described the use of a flumazenil infusion. He appears to have misunderstood the point of the paper. The use of the benzodiazepine antagonist prevented an unnecessary period of prolonged artificial ventilation of the lungs and avoided the many risks (and costs) of this procedure. It was not given as he suggests merely to make him cough. Furthermore Roche Products Ltd kindly donated all of the drug for this patient.

Flumazenil became available to us approximately 2 years ago and we have become increasingly aware of how long the depressant effects of benzodiazepines can persist in critically ill patients, even after small doses (less than 10 mg/day). This may result in some weak patients in the early reinstitution of artificial ventilation, which could be avoided with flumazenil. We are aware of the cost of this agent and partly because of this we have recently used intermittent bolus administration of flumazenil in five patients instead of an infusion. All five patients, who were ready for weaning from artificial ventilation, had gestured that they wanted their tracheal tubes removed because of discomfort. They all became drowsy when their tracheal tubes were removed (presumably because the discomfort was now removed) and started to develop sputum retention. The administration of flumazenil led to a rapid reawakening and clearing of sputum. This effect was transient in all the patients and lasted no more than 30 minutes. The patients could be awoken by a loud voice and there were no signs of airway obstruction, so we assumed the airway was not at risk and decided to leave the patient to doze. Further bolus doses of flumazenil would be administered approximately 4–5 times in each 24-hour period to coincide with times of physiotherapy. We have found flumazenil to be effective and much cheaper used in this way. It remains to be shown that dozing in between times does the patients any harm so long as the airway is not in jeopardy.

The alternatives to this approach include the use of other sedative agents such as propofol (which is not inexpensive) for sedation or the development of transdermal patches of flumazenil (which should be cheaper) or longer acting derivatives of flumazenil. We believe unnecessary artificial ventilation required as a result of the prolonged effects of benzodiazepines is not a safe or cost-effective alternative.

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Anaesthetic induction with isoflurane or halothane

It would be interesting to learn why Phillips, Brimacombe and Simpson (*Anaesthesia* **43:** 927–9) used any nitrous oxide in their work comparing inductions with halothane and isoflurane.

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T.H.S. BURNS

A reply

We thank Dr Burns for his interest in our Article.

It is our normal practice to use nitrous oxide during gaseous induction in children since it accelerates the uptake of the volatile agent by the second gas effect. We wished in addition to be able to make comparisons between our own study and those of the other authors to whom we referred and who had also used nitrous oxide as part of their induction techniques.

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Hearing aid: overlooking the obvious

It is common practice to ensure that the patient has removed his/her own clothing, jewellery and other personal items such as spectacles, contact lenses, dentures and hearing aids before transfer to the operating suite. This is to minimise the risk of loss or damage to these items and to prevent their presence jeopardising the patient's safety during the peri-operative period.

The denial of the use of a hearing aid for patients with hearing difficulties at this time can lead to feelings of isolation, frustration and anxiety. It can also create difficulties for nursing and medical staff since explanations of nursing, anaesthetic and surgical procedures cannot be comprehended. This can inhibit the patient's full cooperation particularly if the procedure is to be carried out under local or regional anaesthesia. Other patients, either waiting to go to theatre or recovering from anaesthesia, can also be disturbed if it is necessary for staff to raise their voice to communicate with a deaf pateint.

These problems can be easily overcome using a piece of equipment readily available in any anaesthetic room, theatre or recovery room: the stethoscope. The patient wears the stethoscope and the medical or nursing attendant can talk in a normal voice into the bell; this improves communication with the patient and avoids disturbance for nearby patients or staff.

This is a very obvious solution to the additional difficulties associated with the deaf patient but it is not one we have previously seen adopted. Perhaps it illustrates the point that the simplest and best solutions to problems are the ones just under our noses.

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Anaesthesia, 1989, Volume 44, pages 367–368

Book reviews

Muscle relaxants in clinical anaesthesia 367
D.R. Bevan, J.C. Bevan and F. Donati
Risk and outcome in anaesthesia 367
Edited by D.L. Brown
Diamorphine: its chemistry, pharmacology and clinical use 368
Edited by D.B. Scott
Books recieved 368

Muscle relaxants in clinical anaesthesia

D.R. Bevan, J.C. Bevan and F. Donati. Pp. x + 443. Year Book Medical, 1988. £35.70.

The authors' stated intent was to provide a review of the current state of knowledge of neuromuscular physiology and pharmacology for the clinician. They have succeeded in many respects, but there are also some disappointing aspects to this book. The contents, which include an entertaining historical discourse are comprehensive and in a reasonably logical sequence. An obvious exception is the chapter on Malignant Hyperthermia. Why was this not incorporated in the excellent chapter on Neuromuscular Diseases and why is it placed between the chapters discussing Succinylcholine and Pharmacology of the Antagonists?

Chapters 2 to 5 deal with the basic physiology and pharmacology of neuromuscular transmission and blockade and are among the best I have read on these topics. The authors obviously have an excellent understanding of what are complex and as yet incompletely understood processes and are able to communicate their knowledge to the reader in simple, but not simplistic, terms. Surprising omissions from these otherwise excellent chapters are references to: the double burst mode of nerve stimulation (chapter 3), the integrated pharmacodynamic model of Sheiner *et al.* (chapter 4) and the gas chromatographic assay for the steroidal muscle relaxants (chapter 5). However, for the clinician who has in the past struggled with the basic scientific aspects of neuromuscular function it is worth buying this book for these chapters alone.

The approach in the later chapters, which deal with the individual agents and the effect of specific disease states on the pharmacology of neuromuscular function, is less successful. The authors give comprehensive reviews of each subject but, because each chapter is so detailed, there is a profusion of information, which makes for much repetition and for tedious reading. The essential information must be gleaned by the reader from a forest of facts. This is in marked contrast to the early chapters where the authors have gone to great pains to extract the essence of each subject and present this to the reader in a lucid concise form. A particular example of the problem is the chapter which discusses Age and Neuromuscular junction. An exception is the chapter on Neuromuscular Diseases which includes a concise and relevant outline for the rational clinical management of the patient with myasthenia gravis.

Three new muscle relaxants, pipecuronium, mivacurium and doxacurium will, in the near future, be introduced into widespread clinical practice. Over the last few years many articles and abstracts about these new drugs have appeared in the literature and I cannot understand why there is no mention of them in this book. These drugs are of obvious interest to the clinician, and not to discuss them at all is a severe deficiency of the book.

The fact that the number of authors is small and that they are all from the same centre, Montreal, has both advantages and disadvantages. There is a consistency of approach which makes for an easy transition between chapters. However, there are some topics which are overemphasised and some which are deficient. An example of the former is the excessive emphasis of the use of combinations of non-depolarising relaxants and of the latter, a paucity of discussion on the very real clinical problem of inadequate reversal of neuromuscular blockade.

The book is abundantly supplied with clear and appropriate illustrations. The list of references is extensive, which makes the book an excellent resource for anyone wishing to explore the subject in greater depth. Overall, I consider that the book deserves to be in the library of every anaesthesia department.

J.E. Caldwell

Risk and outcome in anaesthesia

Edited by D.L. Brown. Pp. 418. Harper and Row, 1988. £35.

Risks and outcome in anaesthesia is a book that has the specific objective of attempting to quantify the risks involved in anaesthetising patients for specific types of surgery and patients with pre-existing disease who undergo a variety of surgical procedures. The first chapter is an historical review of anaesthesia and its risks and the subsequent chapters deal with peri-operative risk in almost all branches of anaesthesia and intensive care. Obvious topics are covered, such as the risks involved in patients with cardiovascular and pulmonary disease and the risks of obstetric anaesthesia; perhaps more interestingly the risks involved in patients with defects in the haematological and immune function, psychiatric disease and nutrition are also discussed. The book ends with a chapter on anaesthesia and medicolegal outcome from the American point of view but which nevertheless has implications for the British anaesthetist. There are 15 chapters in all, each is written by a different author, and each is well referenced and there is a useful index. Books by multiple authors often lack continuity and some chapters are good whilst others are not so good, with the editor having little opportunity to change the contribution of the individual authors. This book suffers from this problem: some chapters are brief and to-the-point, while others tend to ramble on with the attendant difficulty of extracting the relevant facts. Nevertheless, as the reader progresses through the book, he (she) will appreciate the amount of research that has gone into each chapter. The reader will also be impressed by the very genuine attempt that has been made to quantify risks and outcome; yet it has to be admitted that this proves an almost impossible task in some areas. Lack of available data and the impossibility of conducting proper clinical trials are responsible for this.

The chapter on anaesthetic choice, although interesting in itself, seems to extend its brief beyond that of reviewing risks and outcome in anaesthesia. The chapter on critical care contains a great deal of useful information, particularly about various prognostic score systems, but it is difficult to read and thus it is awkward to extract the relevant information. This comprehensive attempt to evaluate risks and outcome in anaesthesia is an interesting concept, however the reader is left wondering whether a book of 15 chapters and 400 pages is necessary to cover the relevant ground, and perhaps the book might benefit from considerable pruning. In its present form it is useful as a reference work, and anaesthetists preparing for the final F.C. Anaesth. examination might usefully use it as such, but it could not be recommended as standard reading matter.

J.C. EDWARDS

Diamorphine: its chemistry, pharmacology and clinical use

Edited by D.B. SCOTT. Pp. xi + 123. Woodhead-Faulkner, 1988. £27.50.

How pleasant to come across a monograph that not only contains information relevant to a wide readership, but is also well presented.

This is a quality book, well laid out and printed on good paper with a leisurely and spacious feel to it. This is due in part to a relatively large print face and wide margins. The book is published by Woodhead-Faulkner as a commission from Evans Medical and if the above qualities are a result of this support then one must welcome the collaboration.

The book contains contributions from 11 authors under the editorship of Bruce Scott. Inevitably some of the chapters are a little general, but this does not detract from the book, more the title. The first two chapters, which deal with the chemistry and pharmacokinetics of the drug, are the best chapters in the book and contain much information not readily available elsewhere. In particular the data on the stability of diamorphine solutions are relevant and helpful. Hull then deals with the pharmacodynamics of the drug in typically lucid and dogmatic fashion that includes a too brief section on mode of action. Scott contributes a simplistic treatise on diamorphine in acute pain, followed by Doyle on Opioids in terminal cancer. The latter is as good a chapter on its title as you can find, but is only occasionally relevant to diamorphine. This detracts somewhat for the specialist. Kaufman then deals with spinal use of the drug in an unbalanced and anecdotal account with little reference to basic scientific data. This is an area which merits profound treatment, with a contribution from a basic scientist as well as a clinician. The last two chapters deal with overdosage and addiction; appropriate to the general topic but less relevant to the anaesthetist.

The book is well edited with little repetition or contradiction, although there is some disagreement about the pharmacological activity of 6-acetylmorphine. The important chapters are well referenced, although given the scope of the book it is inevitable that many references crop up time and again. The index seems adequate and there are a few line drawings, mostly reproduced from scientific papers. These are well reproduced but add little.

I enjoyed this useful book and it will sit easily on my bookshelf. It may not be delved into particularly frequently, but will be recommended to colleagues in the business, and loaned to the rotating pain clinic registrars.

C.E. PITHER

Books received

We thank the publishers for the following books, some of which may be reviewed in future issues of *Anaesthesia.*

Pocket manual of anesthesia.
G. LENZ, B. KOTTLER, R. SCHORER AND W.E. SPOEREL. Pp. xi + 318. Blackwell Scientific, 1988. £14.50.

Baillière's Clinical Anaesthesiology, vol. 2, No. 1 Clinical research in anaesthesia.
Guest editors D.E.F. NEWTON AND N.R. WEBSTER. Pp. ix + 241. Ballière Tindall, 1988. £15.00

Acupuncture, trigger points and musculoskeletal pain.
P.E. BALDRY. Pp. viii + 295. Churchill Livingstone, 1988. £27.50.

Pediatric cardiac anesthesia.
Edited by C.L. LAKE. Pp. xi + 452. Appleton and Lange. £69.55.

Anaesthesia, 1989, Volume 44, pages 369–372

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for December 1988. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

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The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Complications

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Obstetric anaesthesia and analgesia

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Cardiovascular system

Physiology

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Treatment and medication

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Treatment and medication

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Central nervous system

Physiology

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Treatment and medication

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Treatment of obesity: an overview. Bray GA, Gray DS, *Diabetes/Metabolism Reviews* 1988; **4:** 653.

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Diabetic ketoacidosis and hyperosmolar hyperglycemic nonketotic coma. Kitabchi AE, Murphy MB. *Medical Clinics of North America* 1988; **72:** 1545.

Metabolic effects of low-dose insulin therapy on glucose metabolism in diabetic ketoacidosis. Luzi L, Barrett EJ *et al. Diabetes* 1988; **37:** 1470.

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Metabolic effects of hydrochlorothiazide and enalapril during treatment of the hypertensive diabetic patient—enalapril for hypertensive diabetics. Prince MJ, Stuart CA *et al. Archives of Internal Medicine* 1988; **148:** 2363.

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Management of noninsulin-dependent diabetes mellitus. Zimmerman BR, Service FJ. *Medical Clinics of North America* 1988; **72:** 1355.

Pain

Physiology

A study of central neurotransmitter mechanisms in morphine-induced 'straub reaction' in mice. Role of central dopamine receptors. Gupta ML, Nath R *et al. Clinical and Experimental Pharmacology and Physiology* 1988; **15:** 727.

Opioid peptides and substance-P in the cerebrospinal fluid—regulation and significance to pain. Nyberg F, Vaeroy H, Terenius L. In: Olesen J, Edvinsson L, eds. *Basic mechanisms of headache. Amsterdam: Elsevier,* 1988: 241.

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Treatment and medication

Anxiety, pain and sedation—some psychiatric aspects. Mindus P. *Acta Anaesthesiologica Scandinavica* 1988; **32** (Suppl. 88): 7.

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Obituaries

Binning, Rex Austin, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at Brighton Health Authority. Qualified from Cambridge and St George's Hospital, London in 1934.

Crawford, Jeffrey Selwyn, MB, ChB, FRCOG, FFARCS, formerly Consultant Anaesthesist at The Maternity Hospital, Birmingham. Qualified from the University of Leeds in 1947.

English, John Howard, FFARCS, formerly Consultant Anaesthetist in The Netherlands. Qualified from University of Dublin in 1959.

Forrest, Thomas MB, ChB, FFARCS, formerly Administrative Consultant Anaesthetist at Walton and Fazakerley Hospitals, Liverpool. Qualified from University of Glasgow in 1953.

Gibson, John Baird, MB, ChB, FFARCS, DA, formerly Consultant Anaesthetist at the Northumberland Health Authority. Qualified from Glasgow University in 1946.

Hewitt, Andrew Joseph, MB, BCh, BAO, FFARCS, Registrar in Anaesthetics at Waveney Hospital, Ballymena. Qualified from Queen's University, Belfast in 1981.

Leaming, Douglas Leslie, MRCS, LRCP, FFARCS, DA, Consultant Anaesthetist at North Tees General Hospital, Stockton on Tees. Qualified from St Mary's Hospital, London in 1968.

Montgomerie, James, MB, ChB, FFARCS, DA, formerly Consultant Anaesthetist at Bath Clinical Area. Qualified from Birmingham University in 1933.

Organe, Professor Sir Geoffrey Stephen William, MD, FRCS, FFARCS, DA, Emeritus Professor of Anaesthetics, Westminster Medical School, London. Qualified from University of London in 1933. (A full notice will appear later).

International congress calendar

1989

13–15 April. Aruba. *Critical Care in the 1990s.*
Information: Omar Prakash, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

13–15 April. Yamaguchi City, Japan. *Annual Meeting of the Japan Society of Anesthesiology.*
Information: Dr M. Fujita, 5F TY Building, 18–11 Hongo Chome 3, Bunkyo-Ku, Tokyo 113, Japan.

1–3 May. Salzburg, Austria. *Second International Symposium on Echocardiography and Doppler in Cardiac Surgery.*
Information: Dr G. Maurer or Dr W. Mohl, c/o Interconvention, A-1450 Vienna, Austria.

7–12 May. London and Oxford. *The California Society of Anesthesiologists Scientific Meeting in England.*
Information: California Society of Anesthesiologists, 1065 E. Hillsdale Boulevard, Suite 410, Foster City, California 94404-1615, USA.

7–12 May. Melbourne, Australia. *Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Meeting.*
Information: Administrative Officer, Faculty of Anaesthetists, RACS, Spring Street, Melbourne, Victoria 3000.

10–13 May. Rotterdam, The Netherlands. *Second European Congress of Paediatric Anaesthesia.*
Information: Congress Secretariat, V.V.V., Rotterdam Tourist Office, Coolsingel 67, NL 3012 AC Rotterdam.

11–14 May. Rotterdam. *Second European Congress of Paediatric Anaesthesia.*
Information: Mrs J.F. Aukes-Jager, Sophia Children's Hospital, Department of Paediadric Anaesthesia, Gordelweg 160, NL-3038 GE, Rotterdam.

17–19 May. Lisbon. *VIII Annual Meeting of the European Society of Regional Anaesthesia.*
Information: Dr E. Lopes Soares, Rua Cidade de Cadiz 14, 1500 Lisboa.

26–27 May. Cottbus. *III Bilaterales Anaesth. Schwesternsymposium DDR/CSSR.*
Information: Dr K.-H. Pickart, Karowerstr. 11, DDR-1115 Berlin-Buch, DDR.

26–27 May. Paris. *7th International Meeting of MAPAR.*
Information: MAPAR, Corinne de Maindreville, Hopital Bicetre, F-94275 Le Kremlin Bicetre, Cedex France.

2–9 June. Paris, France. *Paris in the Spring, Meeting for Anesthesiologists Information:* G. Silvay, MD, PhD, Mount Sinai School of Medicine, Box 1010, 1 Gustave L. Levy Place, New York, NY 10029, USA.

9–12 June. Florida. *Twelfth Annual Conference of the Shock Society.*
Information: Shock Society Office, c/o Dr S.M. Reichard, Medical College of Georgia, Augusta, GA 30912, USA.

9–13 June. Ottawa. *Joint Meeting of the Canadian Anaesthetists' Society with the Association of Anaesthetists of Great Britain and Ireland.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

26–30 June. Copenhagen. *20th Scandinavian Congress.*
Information: Professor S.H. Johansen, Herlev Hospital, DK 2730, Herlev, Denmark.

13–15 July. London. *Refresher Course and Scientific Meeting of European Academy of Anaesthesiologists.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

12–16 August. Christchurch. *Combined Meeting of New Zealand Society with the Australian Society of Anaesthetists.*
Information: Secretariat, ASA NZ Society of Anaesthetists, P.O. Box 600, Edgecliffe, NSW 2027, Australia.

23–25 August. Oulu, Finland. *Scandinavian Meeting of the European Society of Regional Anaesthesia.*
Information: Secretariat, Scandinavian ESRA, Department of Anaesthesia, University of Oulu, SF 90220 Oulu, Finland.

30 August–2 September. Bonn, West Germany. *11th Annual Meeting of European Academy.*
Information: Professor Dr H. Stoeckel, Institut fur Anaesthesiologie der Rheinischen Friedrich-Wilhelm-Universitat, Sigmund Freud Str. 25, D 5300, Bonn 1.

1–4 September. Tunisia. *3rd Pan Arab Congress of Anaesthesia and Intensive Care.*
Information: Dr Jamal Al-Shanableh, P.O. Box 15404, Marka-Amman, Jordan.

3–8 September. Kyoto, Japan. *Fifth World Congress on Intensive and Critical Care Medicine.*
Information: The Fifth World Congress on Intensive and critical Care Medicine, c/o Japan Convention Services Inc., Nippon Press Center Building 2-2-1 Uchisaiwai-cho, Chiyoda-ku, Tokyo 100, Japan.

7–9 September. Arusha Tanzania. *Annual Scientific Conference of the Society of Anaesthesiologists of East Africa.*
Information: Dr H. Lweno, P.O. Box 7097, Dar Es Salaam, Tanzania.

10–14 September. Freiburg. *8th Congress of European Society of Pneumology.*

Information: Professor Dr med. H. Matthys, Arztlicher Direktor, Abteilung Pneumologie, Robert-Koch-Klinik, Universitat, D 7800 Freiburg, West Germany.

10–15 September. Hong Kong. *6th World Congress on Emergency and Disaster Medicine.*
Information: Dr M. Moles, c/o Meeting Planners, 701 Tung Wai Comm Bldg, 109 Gloucester Road, Wanchai, Hong Kong.

12–16 September. Austria. *International Conference on Anaesthesia, Intensive Care and Emergency Medicine.*
Information: Professor Dr J.M. Hackl, University Klinik fur Anaesthesia und Allg. Intensivmedizin, Ahichstr. 35, A-6020, Innsbruck, Austria.

13–15 September. Swansea. *Linkman Conference and Annual Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

14–15 September. Osaka, Japan. *4th International Symposium of Endocrinology in Anaesthesia and Surgery.*
Information: Department of Anesthesiology, University of Hirosaki, School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori-ken, 036 Japan.

16–19 September. Herzliya, Israel. *The Second International Symposium–Pain 1989.*
Information: Pain 1989 Secretariat, P.O. Box 50006, Tel Aviv 61500, Israel.

17–19 September. Beijing. *1st International Symposium on Emergency Medicine.*
Information: Dr M. Moles, c/o Meeting Planners, 701 Tung Wai Comm Bldg., 109 Gloucester Road, Wanchai, Hong Kong.

18–22 September. London. *9th Congress of the Federation Internationale de Medecine Manuelle.*
Information: Conference Associates FIMM, 27A Medway Street, London, SW1P 2BD.

19–22 September. Tel Aviv. *15th International Congress of the Israel Society of Anesthesiologists.*
Information: Anesthesiologists 1989, P.O. Box 50006, Tel Aviv 61500, Israel.

27–30 September. Warsaw. *Joint Meeting between Association of Paediatric Anaesthetists of Great Britain and Ireland and Polish Society.*
Information: Dr J. Kacki, ul Kasprzaka 17A, 01–211 Warsaw, Poland.

4–7 October. Tunis. *Third Pan Arab Congress on Anaesthesia and Intensive Care.*
Information: Secretary, P.O. Box 15404, Marka, Amman, Jordan.

14–18 October. New Orleans. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

18–20 October. Barcelona. *11th Congress of Chronical Roncopathy.*
Information: BRP, Edificio Layetana C-Pau Claris, 138, 08009, Barcelona, Spain.

26–28 October. Berlin. *3rd International Steglitz Symposium on Clinical aspects of O_2 transport and tissue oxygenation.*
Information: M. Specht, Klinik fur Anaesthesiologie und operative Intensivmedizin, Klinikum Steglitz FU-Berlin, Hindenburgdamm 30, D-1000 Berlin 45.

18–22 October. Tokyo and Kyoto. *6th World Congress for Bronchology.*
Information: Dr M. Niitsuma, Secretary General, 6th World Congress for Bronchology, Department of Surgery, Tokyo Medical College, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160 Japan.

3–5 November. Toronto, Canada. *Paediatric Anaesthesia Conference.*
Information: Paediatric Anaesthesia Conference, The Hospital for Sick Children, 555 University Avenue, Toronto, Ont. M5G 1X8, Canada.

5–10 November. Sao Paulo. *36th Brazilian Congress of Anesthesiology.*
Information: Congress Secretariat, Dr R.S. Nathias, Rua Caiubi 666, Sao Paulo, Brazil 05010.

11–17 November. River Rhine. *International Symposium to commemorate '60 years of surfactant research'.*
Information: Professor B. Lachmann, Department of Anesthesiology, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

28 November–1 December. Manila. *6th ASEAN Congress of Anaesthesiologists.*
Information: P.O. Box 4486, Manila, Philippines.

1990

24–26 February. New Orleans. *Mardi Gras Anaesthetic Course.*
Information: Alan Grogono, Tulane University Medical Center, 1430 Tulane Avenue, New Orleans, Louisiana 70112, USA.

10–14 March. Honolulu. *64th Congress of the International Anaesthesia Research Society.*
Information: Emerson A. Moffitt, IARS, 3645 Warrendsville Center Road, Cleveland, Ohio 44122, USA.

18–23 March. Durban, South Africa. *National Anaesthetic Congress of the South African Society of Anaesthetists.*
Information: Professor D.A. Rocke, University of Natal, Department of Anaesthetics, Medical School, P.O. Box 17039, Congella, Durban, South Africa, 4013.

27–30 March. Brussels. *10th International Symposium on Intensive Care and Emergency Medicine.*
Information: Dr J.L. Vincent, Dept. of Intensive Care, Erasme University Hospital, Route de Lennik 808, 1070 Brussels, Belgium.

4–6 April. Glasgow. *Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

13–19 May. Wellington, New Zealand. *Faculty of Anaesthetics and the Royal Australasian College of Surgeons Annual General Meeting.*
Information: Administrative Officer, Faculty of Anaesthetists, RACS, Spring Street, Melbourne, Victoria 3000.

15–19 June. Vancouver. *47th Annual Meeting of the Canadian Anaesthetists' Society.*
Information: Ms Ann Andrews, CAS 187, Gerrard St. E, Toronto, Ontario M5A 2E5 Canada.

9–15 September. Warsaw. *VIIIth European Congress of Anaesthesiologie.*
Information: The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o The Polish Society of Anaesthesiology and Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

23–28 September. Seoul. *8th Asian/Australasian Congress of Anaesthesia.*
Information: Department of Anesthesiology, Seoul National University Hospital 28 Yungun-Dong, Chongro-Ku, Seoul 110.

26–28 September. Manchester. *Linkman Conference and Annual Scientific Meeting Exhibition.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

19–23 October. Las Vegas. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

5–10 November. Sao Paulo. *36th Brazilian Congress of Anesthesiology.*
Information: Dr R. Mathias, Rua Caiubi 666, Sao Paulo, Brazil 05010.

5–9 December. San Juan. *15th Caribbean Symposium in Anaesthesia and Related Fields.*
Information: Miguel Colon-Morales, GPO Box 4547, San Juan, Puerto Rico 00936.

1991

8–12 March. San Antonio. *65th Congress of the International Anesthesia Research Society.*
Information: Emerson A. Moffitt, IARS, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

9–12 May. Washington DC. *6th International Dental Congress on Modern Pain Control.*
Information: American Dental Society of Anesthesiology, Inc., 211 E. Chicago Avenue, Suite 948, Chicago, IL 60611.

21–25 June. Quebec City. *48th Annual Meeting of Canadian Anaesthetists' Society.*

Information: Ms Ann Andrews, CAS, 187 Gerrard St. E., Toronto, Ontario M5A 2E5, Canada.

26–30 October. San Francisco. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

1992

29 March–2 April. Atlanta, Georgia. *The Third International Symposium on the History of Anaesthesia.*
Information: R.K. Calverley, Medical Center, University of California, 225 Dickinson Street, San Diego, California CA 92103, 1990, USA.

14–19 June. The Hague. *10th World Congress of Anaesthesiology.*
Information: Dr Harm Lip, Nilantsweg, 99, 8041 AR Zwolle, Netherlands.

17–21 October. New Orleans. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

1993

15–17 September. Glasgow. *Joint Meeting with the Canadian Society of Anaesthetists.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

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The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.
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BOOKS AND OTHER MONOGRAPHS

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Corporate authors
American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author
Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences,* 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book
Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication
National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article
Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

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